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CONTENTS OF VOLUME 19

JULY, 1929. NUMBER 1

Surgical Applications of Therapeutic Venous Obstruction. Barney Brooks, M.D., Nashville, Tenn.....	1
The Structure of Bone, with Particular Reference to Its Fibrillar Nature and the Relation of Function to Internal Architecture. Henry L. Jaffe, M.D., New York	24
Surgery of the Esophagus. James H. Saint, M.D. (Durham), M.R.C.S., L.R.C.P., Rochester, Minn.....	55
A New Abdominal Incision. J. Tate Mason, M.D., Seattle.....	129
Operative Relief from Pain in Lesions of the Mouth, Tongue and Throat. Walter E. Dandy, M.D., Baltimore.....	143
Bronchobiliary Fistula. M. G. Seelig, M.D., and J. J. Singer, M.D., St. Louis.....	149
Endometrioma of the Terminal Ileum, Appendix and Cecum. F. N. G. Starr, C.B.E., M.B., Toronto.....	152
Thirty-Eighth Report of Progress in Orthopedic Surgery. Philip D. Wilson, M.D.; Lloyd T. Brown, M.D.; M. N. Smith-Petersen, M.D.; Ralph Ghormley, M.D.; John Kuhns, M.D., and Edward Cave, M.D., Boston; Murray S. Danforth, M.D., Providence, R. I.; C. Herman Bucholz, M.D., Halle, Germany; George Perkins, London, England, and Arthur Van Dessel, M.D., Louvain, Belgium.....	154

AUGUST, 1929. NUMBER 2

Osteitis Fibrosa and Giant Cell Tumor. Charles F. Geschickter, M.D., and Murray M. Copeland, M.D., with Foreword by Joseph Colt Bloodgood, M.D., Baltimore	169
The Relation of the Adrenal Gland to the Toxemia of Intestinal Obstruction: An Experimental Study. R. A. Cutting, M.D., Ph.D., New Orleans....	272
Acute Complete Obstruction of the Duodenum Following a Gastrojejunostomy: Cure by Degastro-Enterostomy. John E. Summers, M.D., Omaha.....	292
Pericardotomy for Pyopericardium. L. G. Bowers, M.D., Dayton, Ohio....	301
Ganglioneuroma of Mediastinum Requiring Surgical Intervention for Relief of Obstructive Symptoms. T. F. Riggs, M.D., and L. P. Good, M.D., Pierre, S. D.....	309
Variations in the Extrahepatic Biliary Tract. Meredith G. Beaver, M.D., Rochester, Minn.	321
A Review of Urologic Surgery. Albert J. Scholl, M.D., Los Angeles; E. Starr Judd, M.D., Rochester, Minn.; Linwood D. Keyser, M.D., Roanoke, Va.; Gordon S. Foulds, M.D., Toronto, Canada; Jean Verbrugge, M.D., Antwerp, Belgium, and Adolph A. Kutzmann, M.D., Los Angeles	327

CONTENTS OF VOLUME 19

SEPTEMBER, 1929. NUMBER 3

	PAGE
Traumatic Subclavian Arteriovenous Aneurysm: Final Report. Edgar Lorington Gilcreest, M.D., San Francisco.....	375
The Celiac Plexus and Its Branches. F. Kiss, M.D., Budapest, Hungary, and Harry C. Ballou, M.D., St. Louis.....	399
The Branchial Apparatus: Its Embryologic Origin and the Pathologic Changes to Which It Gives Rise, with Presentation of a Familial Group of Fistulas. Olan R. Hyndman, M.D., and George Light, M.D., Iowa City	410
Lymphatic Drainage from the Peritoneal Cavity in the Dog. George M. Higgins, Ph.D., and A. Stephens Graham, M.D., Rochester, Minn.....	453
Old Nodular Goiter Surrounding Trachea, Posterior to the Carotid with the Isthmus Posterior to the Esophagus: Report of a Case with Sudden Death from Acute Abscess. Miles F. Porter, M.D., Fort Wayne, Ind.	466
The Effect of Intrabronchial Injections of Iodized Poppy Seed Oil 40 Per Cent: An Experimental Study on Dogs. Ralph Boerne Bettman, M.D.; John Kelly, M.D., and Nathan Crohn, M.D., Chicago.....	471
Intestinal Obstruction: Experimental Studies on Toxicity, Intra-Intestinal Pressure and Chloride Therapy. Forrester Raine, M.D., and Margaret C. Perry, M.A., Milwaukee.....	478
A Comparative Study of the Bactericidal Values of Twenty-One Commonly Used Antiseptics. Abbott William Allen, M.D., New York.....	512
Surgical Diseases of the Colon: Cooperative Management. Fred W. Rankin, M.D., and J. Arnold Borgen, M.D., Rochester, Minn.....	518
A Review of Abdominal Surgery. Gunther W. Nagel, M.D., San Francisco; E. Starr Judd, M.D., Rochester, Minn.; Bennett R. Parker, M.D., Chicago; Winfred H. Bueermann, M.D., Portland, Ore., and H. Peiper, M.D., Frankfurt Am Main, Germany.....	526

OCTOBER, 1929. NUMBER 4

Air Embolism from the Pulmonary Vein: A Clinical and Experimental Study. C. M. Van Allen, M.D., and L. S. Hrdina, Chicago, and J. Clark, M.D., Iowa City.....	567
Experimental Peptic Ulcer. James C. McCann, M.D., Rochester, Minn.....	600
Loose Cartilage from Intervertebral Disk Simulating Tumor of the Spinal Cord. Walter E. Dandy, M.D., Baltimore.....	660
Renal Counterbalance. James J. Joelson, M.D.; Claude S. Beck, M.D., and Alan R. Moritz, M.D., Cleveland.....	673
The Delbet Apparatus and the End-Results. Edward T. Crossan, M.D., Philadelphia	712
Trauma to Central Nervous System: Its Effects on Cardiac Output and Blood Pressure. An Experimental Study. Alfred Blalock, M.D., and Hubert B. Bradburn, M.D., Nashville, Tenn.....	725
Thrombo-Angiitis Obliterans: General Distribution of the Disease, Maurice E. Barron, M.D., and Harry Linenthal, M.D., Boston.....	735

CONTENTS OF VOLUME IV

OCTOBER—Continued

Thirty-Ninth Report of Progress in Orthopedic Surgery. Phil. D. Wilson, M.D.; Lloyd T. Brown, M.D.; M. N. Smith-Petersen, M.D.; Paul Ghormley, M.D.; John Kuhns, M.D., and Edward Cave, M.D., Philadelphia; Murray S. Danforth, M.D., Providence, R. I.; George Perkins, M.D., England, and Arthur Van Dessel, M.D., Louvain, Belgium	75
---	----

NOVEMBER, 1929. NUMBER 5

Correlations of Internal and External Pancreatic Secretion	
I. General Considerations and Review of the Literature. G. de Takats, M.D., Chicago	271
II. The Histologic Changes in the Isolated Tail of the Pancreas. G. de Takats, M.D., Chicago	277
III. The Effect of Ligation of the Tail of the Pancreas on Dog Blood. G. de Takats, M.D., and I. T. Nathanson, D.S., Chicago	287
Experimental Sarcoma of Bone. Charles I. Connor, M.D., San Francisco	294
Pulmonary Atelectasis and Respiratory Failure. Israel Rosenberg, M.D., New York	300
Cavernous Hemangioma of the Scrotum: Report of a Case. Nathan Winkler, M.D., Baltimore	302
Surgical Wounds in Human Beings: A Histologic Study of Healing and Practical Applications; I. Epithelial Healing. Shattuck W. Henshaw, M.D., Rochester, Minn.	315
Primary Carcinoma of the Fallopian Tube: A Series of Fourteen Cases. Lawrence R. Wharton, M.D., Baltimore, and F. H. Krook, M.D., Fort Smith, Ark.	318
Leukoplakia of the Renal Pelvis. Adolph A. Kutzmann, M.D., Los Angeles	371
Oxygen Content of Blood in Patients with Varicose Veins. Alfred Blahosky, M.D., Nashville, Tenn.	388
Carcinoma of the Colon: Intraperitoneal Vaccination by Mixed Vaccine of Colon Bacilli and Streptococci. Fred W. Rankin, M.D., and J. Arnold Bargen, M.D., Rochester, Minn.	391
Acute Obstruction of the Small Intestine Due to a Gallstone: Recovery Following Operation. Golder L. McWhorter, M.D., Ph.D., Chicago	395
A Review of Urologic Surgery (to be Continued). Albert J. Scholl, M.D., Los Angeles; E. Starr Judd, M.D., Rochester, Minn.; Linwood D. Keyser, M.D., Roanoke, Va.; Gordon S. Foulds, M.D., Toronto, Canada; Jean Verbrugge, M.D., Antwerp, Belgium, and Adolph A. Kutzmann, M.D., Los Angeles	322

DECEMBER, 1929. PART I. NUMBER 6

Value of Blood Amylase Estimations in the Diagnosis of Pancreatic Disease: A Clinical Study. Robert Elman, M.D.; Norman Arneson, M.D., and Evarts A. Graham, M.D., St. Louis	943
Fractures of the Transverse Processes of the Lumbar Vertebrae: A Report of Thirty-Three Cases. Paul A. Quaintance, M.D., Los Angeles	968
Gross and Microscopic Structure of the Thyroid Gland in Man. William Francis Rienhoff, Jr., M.D., Baltimore	986
The Gallbladder: Its Functions and Some of Their Disturbances in the Light of Recent Investigations. Béla Halpert, M.D., Chicago	1037

CONTENTS OF VOLUME 19

SEPTEMBER, 1929. NUMBER 3

	PAGE
Traumatic Subclavian Arteriovenous Aneurysm: Final Report. Edgar Lorington Gilcreest, M.D., San Francisco.....	375
The Celiac Plexus and Its Branches. F. Kiss, M.D., Budapest, Hungary, and Harry C. Ballou, M.D., St. Louis.....	399
The Branchial Apparatus: Its Embryologic Origin and the Pathologic Changes to Which It Gives Rise, with Presentation of a Familial Group of Fistulas. Olan R. Hyndman, M.D., and George Light, M.D., Iowa City	410
Lymphatic Drainage from the Peritoneal Cavity in the Dog. George M. Higgins, Ph.D., and A. Stephens Graham, M.D., Rochester, Minn.....	453
Old Nodular Goiter Surrounding Trachea, Posterior to the Carotid with the Isthmus Posterior to the Esophagus: Report of a Case with Sudden Death from Acute Abscess. Miles F. Porter, M.D., Fort Wayne, Ind.	466
The Effect of Intrabronchial Injections of Iodized Poppy Seed Oil 40 Per Cent: An Experimental Study on Dogs. Ralph Boerne Bettman, M.D.; John Kelly, M.D., and Nathan Crohn, M.D., Chicago.....	471
Intestinal Obstruction: Experimental Studies on Toxicity, Intra-Intestinal Pressure and Chloride Therapy. Forrester Raine, M.D., and Margaret C. Perry, M.A., Milwaukee.....	478
A Comparative Study of the Bactericidal Values of Twenty-One Commonly Used Antiseptics. Abbott William Allen, M.D., New York.....	512
Surgical Diseases of the Colon: Cooperative Management. Fred W. Rankin, M.D., and J. Arnold Borgen, M.D., Rochester, Minn.....	518
A Review of Abdominal Surgery. Gunther W. Nagel, M.D., San Francisco; E. Starr Judd, M.D., Rochester, Minn.; Bennett R. Parker, M.D., Chicago; Winfred H. Bueermann, M.D., Portland, Ore., and H. Peiper, M.D., Frankfurt Am Main, Germany.....	526

OCTOBER, 1929. NUMBER 4

Air Embolism from the Pulmonary Vein: A Clinical and Experimental Study. C. M. Van Allen, M.D., and L. S. Hrdina, Chicago, and J. Clark, M.D., Iowa City.....	567
Experimental Peptic Ulcer. James C. McCann, M.D., Rochester, Minn.....	600
Loose Cartilage from Intervertebral Disk Simulating Tumor of the Spinal Cord. Walter E. Dandy, M.D., Baltimore.....	660
Renal Counterbalance. James J. Joelson, M.D.; Claude S. Beck, M.D., and Alan R. Moritz, M.D., Cleveland.....	673
The Delbet Apparatus and the End-Results. Edward T. Crossan, M.D., Philadelphia	712
Trauma to Central Nervous System: Its Effects on Cardiac Output and Blood Pressure. An Experimental Study. Alfred Blalock, M.D., and Hubert B. Bradburn, M.D., Nashville, Tenn.....	725
Thrombo-Angiitis Obliterans: General Distribution of the Disease, Maurice E. Barron, M.D., and Harry Linenthal, M.D., Boston.....	735

CONTENTS OF VOLUME 19

OCTOBER—Continued

PAGE

- Thirty-Ninth Report of Progress in Orthopedic Surgery. Philip D. Wilson, M.D.; Lloyd T. Brown, M.D.; M. N. Smith-Petersen, M.D.; Ralph Ghormley, M.D.; John Kuhns, M.D., and Edward Cave, M.D., Boston; Murray S. Danforth, M.D., Providence, R. I.; George Perkins, London, England, and Arthur Van Dessel, M.D., Louvain, Belgium..... 752

NOVEMBER, 1929. NUMBER 5

Correlations of Internal and External Pancreatic Secretion:

- I. General Considerations and Review of the Literature. G. de Takats, M.D., Chicago 771
 - II. The Histologic Changes in the Isolated Tail of the Pancreas. G. de Takats, M.D., Chicago..... 775
 - III. The Effect of Ligation of the Tail of the Pancreas on Diastase in the Blood. G. de Takats, M.D., and I. T. Nathanson, B.S., Chicago..... 788
- Experimental Sarcoma of Bone. Charles L. Connor, M.D., San Francisco.. 794
- Pulmonary Atelectasis and Respiratory Failure. Israel Rappaport, M.D., New York 804
- Cavernous Hemangioma of the Scrotum: Report of a Case. Nathan Winslow, M.D., Baltimore 829
- Surgical Wounds in Human Beings: A Histologic Study of Healing with Practical Applications; I. Epithelial Healing. Shattuck W. Hartwell, M.D., Rochester, Minn..... 835
- Primary Carcinoma of the Fallopian Tube: A Series of Fourteen Cases. Lawrence R. Wharton, M.D., Baltimore, and F. H. Krock, M.D., Fort Smith, Ark. 848
- Leukoplakia of the Renal Pelvis. Adolph A. Kutzmann, M.D., Los Angeles 871
- Oxygen Content of Blood in Patients with Varicose Veins. Alfred Blalock, M.D., Nashville, Tenn..... 898
- Carcinoma of the Colon: Intraperitoneal Vaccination by Mixed Vaccine of Colon Bacilli and Streptococci. Fred W. Rankin, M.D., and J. Arnold Bargen, M.D., Rochester, Minn..... 906
- Acute Obstruction of the Small Intestine Due to a Gallstone: Recovery Following Operation. Golder L. McWhorter, M.D., Ph.D., Chicago. 915
- A Review of Urologic Surgery (to be Continued). Albert J. Scholl, M.D., Los Angeles; E. Starr Judd, M.D., Rochester, Minn.; Linwood D. Keyser, M.D., Roanoke, Va.; Gordon S. Foulds, M.D., Toronto, Canada; Jean Verbrugge, M.D., Antwerp, Belgium, and Adolph A. Kutzmann, M.D., Los Angeles 922

DECEMBER, 1929. PART I. NUMBER 6

- Value of Blood Amylase Estimations in the Diagnosis of Pancreatic Disease: A Clinical Study. Robert Elman, M.D.; Norman Arneson, M.D., and Evarts A. Graham, M.D., St. Louis..... 943
- Fractures of the Transverse Processes of the Lumbar Vertebrae: A Report of Thirty-Three Cases. Paul A. Quaintance, M.D., Los Angeles..... 968
- Gross and Microscopic Structure of the Thyroid Gland in Man. William Francis Rienhoff, Jr., M.D., Baltimore..... 986
- The Gallbladder: Its Functions and Some of Their Disturbances in the Light of Recent Investigations. Béla Halpert, M.D., Chicago.....1037

DECEMBER, PART I--Continued

PAGE

Fibroma of the Vulva Containing an Epithelial Inclusion Cyst. Leo Brady, M.D., Baltimore	1061
Experimental Ileus: I. High Obstruction with the Biliary, Pancreatic and Duodenal Secretions Short-Circuited Below the Obstructed Point. Tilger Perry Jenkins, M.D., Chicago.....	1072
Localization of Bacteria in Tissues of Lowered Resistance. W. Warren Sager, M.D., and Allen C. Nickel, M.D., Rochester, Minn.....	1086
A Review of Urologic Surgery (Concluded). Albert J. Scholl, M.D., Los Angeles; E. Starr Judd, M.D., Rochester, Minn.; Linwood D. Keyser, M.D., Roanoke, Va.; Gordon S. Foulds, M.D., Toronto, Canada; Jean Verbrugge, M.D., Antwerp, Belgium, and Adolph A. Kutzmann, M.D., Los Angeles	1090

DECEMBER, 1929. PART II. NUMBER 6

Report on the Activities of the Chest Tumor Registry.....	1121
Pulmonary Tuberculosis: Pathology and Treatment. John L. Yates, M.D., Milwaukee	1122
Direct Drainage of Tuberculous Pulmonary Cavities. Howard Lilienthal, M.D., New York.....	1161
Phrenicectomy in Three Hundred Cases of Pulmonary Tuberculosis. E. S. Welles, M.D., Saranac Lake, N. Y.....	1169
The Electrosurgical Method of Closed Intrapleural Pneumolysis in Artificial Pneumothorax. Ralph C. Matson, M.D., Portland, Ore.....	1175
Therapeutic Pulmonary Collapse. Dean B. Cole, M.D., and Frank S. Johns, M.D., Richmond, Va.....	1193
The Effects of Closed Pneumothorax and Phrenicotomy on the Cardio-respiratory Function. William DeW. Andrus, M.D., and J. D. Wilson, M.D., Cincinnati	1205
Functional Aspects of Bronchial Muscle and Elastic Tissue. Charles C. Mucklin, M.D., Ph.D., F.R.S.C., London, Canada.....	1212
Cin-Ex Camera Studies of the Tracheobronchial Tree. W. A. Hudson, M.D., and Hans A. Jarre, M.D., Detroit.....	1236
The Production of Intrapulmonary Suppuration by Secondary Infection of a Sterile Embolic Area: An Experimental Study. Emile Holman, M.D., and Mary E. Mathes, M.D., San Francisco.....	1246
Bronchogenic Contamination in Embolic Abscess of the Lungs. C. M. Van Allen, M.D., New Haven, Conn., and W. E. Adams, M.D., and L. S. Hrdina, Chicago	1262
Embolism in Bronchogenic Infection of the Lung. C. M. Van Allen, M.D., New Haven, Conn., and W. E. Adams, M.D., and L. S. Hrdina, Chicago.....	1279
Pulmonary Abscess: An Analysis of One Hundred and Seventy-Two Cases. John B. Flick, M.D.; Louis H. Clerf, M.D.; Elmer H. Funk, M.D., and John T. Farrell, Jr., M.D., Philadelphia.....	1292
A Case of Abscess of the Lung, with Filling of a Cavity and Closure of a Bronchial Fistula by Pedicle Muscle Graft. Francis A. C. Scrimger, M.D., Montreal, Canada	1313

CONTENTS OF VOLUME 19

DECEMBER, PART II—Continued

PAGE

Postoperative Pulmonary Hypoventilation. George P. Muller, M.D.; Richard H. Overholt, M.D., and Eugene P. Pendergrass, M.D., Philadelphia.....	1322
The Circulation in the Compressed, Atelectatic and Pneumonic Lung. (Pneumothorax-Apneumotosis-Pneumonia). Pol N. Coryllos, M.D., and George L. Birnbaum, M.D., New York.....	1346
The Surgical Treatment of Bronchial Asthma. Edgar W. Phillips, M.D., and W. J. Merle Scott, M.D., Rochester, N. Y.....	1425
Decortication of the Heart (Delorme) for Adhesive Pericarditis. Edward D. Churchill, M.D., Boston.....	1457
Sensibility of the Exposed Human Heart and Pericardium. John Alexander, M.D.; A. Garrard Macleod, M.D., and Paul S. Barker, M.D., Ann Arbor, Mich.	1470
Operations on the Innominate Artery: Report of a Successful Ligation. James Greenough, M.D., Cooperstown, N. Y.....	1484
Operations and Demonstrations of Cases in Barnes Hospital:	
1. Thoracoplasty and Phrenicectomy. Evarts A. Graham, M.D., and Duff S. Allen, M.D., St. Louis.....	1545
2. Clinic Demonstrations. Jacob J. Singer, M.D., and Evarts A. Graham, M.D., St. Louis.....	1552
3. Bronchography. Jacob J. Singer, M.D., St. Louis.....	1571
Demonstrations of Experimental Work in the Washington University School of Medicine:	
1. Caliber Changes in the Bronchi in Normal Respiration. Peter Heinbecker, M.D., St. Louis.....	1574
2. Changes in the Shape and Size of the Tracheobronchial Tree Following Stimulation of the Vagosympathetic Nerve. Byron F. Francis, M.D., St. Louis.....	1577
3. Emphysema Simulating Cardiac Decompensation. W. B. Kountz, M.D., and H. L. Alexander, M.D., St. Louis.....	1584
4. Experimental Abscess of the Lung Following Ligation of the Pulmonary Artery and Incision and Suture of the Pulmonary Parenchyma. I. Y. Olch, M.D., and Harry C. Ballon, M.D., St. Louis....	1586
5. The Origin of Scar Tissue in Healing of the Lung. I. Y. Olch, M.D., and Harry C. Ballon, M.D., St. Louis.....	1595
6. The Bacterial Flora of Treated and of Untreated Abscesses of the Lung. Philip L. Varney, M.S., St. Louis.....	1602
7. Early Carcinoma of the Lung. S. H. Gray, M.D., and J. Cordonnier, M.D., St. Louis.....	1618
8. Consequences of Variations in Mediastinal Pressure; Mediastinal and Subcutaneous Emphysema. Harry C. Ballon, M.D., and Byron F. Francis, M.D., St. Louis.....	1627
9. Comparison of Iodized Oil and Brominized Oil. Jacob J. Singer, M.D., and Byron F. Francis, M.D., St. Louis.....	1660
10. Effects of Pressure on the Heart, with Reference to the Advisability of Decompression of Greatly Enlarged Hearts: Experimental Study. Duff S. Allen, M.D., and Evarts A. Graham, M.D., St. Louis.....	1663
11. Cytology of Serous Effusions, with Special Reference to Tumor Cells. Alfred Goldman, M.D., St. Louis.....	1672

CONTENTS OF VOLUME 19

DECEMBER, PART II—Continued

	PAGE
Surgical Treatment of Intrathoracic Tumors. Stuart W. Harrington, M.D., Rochester, Minn.	1679
The Treatment of Some Unusual and Difficult Cases of Empyema. Charles D. Lockwood, M.D., Pasadena, Calif.....	1726
Empyema: Treatment by Tidal Irrigation and Suction. Deryl Hart, M.D., Baltimore	1732
Proceedings	1767
Changes in Constitution and By-Laws.....	1769
List of Members of the American Association for Thoracic Surgery.....	1770
In Memoriam:	
Howard A. Lothrop	1773
Necrology	1774

SURGICAL APPLICATIONS OF THERAPEUTIC VENOUS OBSTRUCTION *

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It is remarkable that a process so apparent as the circulation of the blood could have remained undiscovered through so many centuries during which there was an accumulation of knowledge of other more complex phenomena. If one only contemplates the vast number of opportunities which were presented for the discovery of the circulation of the blood and recalls the simplicity of the experiments of William Harvey, one is amazed that this discovery should have been deferred so long. It would seem as if a sort of mysticism always assigned to the cardiovascular mechanism had prevented an appreciation of its simple realities. Discussions of the problems of the circulation of the extremities still contain many vague ideas and few definite terms. It would seem worth while, therefore, to discuss some therapeutic measure applicable to disease of the circulation of the extremities with the object in view of tracing its historical development and collecting the existent definite knowledge concerning its fundamental principles.

Therapeutic venous obstruction is as old as medical literature. * It is quite natural that intentional obliteration of veins should have been first used in the treatment of conditions in which there were external manifestations of disease in the veins. Hippocrates¹ described a method of obliteration of a varix in which needles were passed into the dilated veins. Paul of Aegina,² Celsus and Galen described methods of excision of varicose veins, and this operation is said to have been mentioned by Pliny and Plutarchus. The fact that the celebrated Caius Marius submitted to an operation for varicose veins without being bound is mentioned as an evidence of his fortitude. In more recent times, Max Schede³ and Trendelenburg⁴ revived the operative treat-

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* From the Department of Surgery, Vanderbilt University Medical School.

* The Hodggen Lecture of the St. Louis Surgical Society, delivered in St. Louis, Jan. 15, 1929.

1. Works of Hippocrates, translated by Francis Adams, New York, William Wood & Company, vol. 2, p. 305.

2. Paulus Aegeneta: New Sydenham Series, 1846, vol. 2, p. 406.

3. Schede, Max: Berl. klin. Wchnschr. 14:85, 1877.

4. Trendelenburg: Beitr. z. klin. Chir. 7:195, 1891.

ment for varicose veins. During the past few years, there has been a marked revival of interest in therapeutic venous occlusion by injection. It is interesting to note that this method was extensively used and discarded previous to the development of antiseptic surgery.

The origination of the idea of purposeful occlusion of normal veins as a therapeutic measure in the treatment for arterial disease is usually ascribed to Sir George Makins⁵ who observed, from experiences in the South African War, that there was a smaller incidence of gangrene in those instances of arteriovenous fistula resulting from gunshot wounds which were treated by ligation of both the artery and the vein than in similar wounds treated by ligation of the artery alone. It is interesting to note, however, that this observation of Makins was not recorded until his delivery of the Bradshaw Lecture in 1913, and that at this time he referred only to a study of a series of records of arteriovenous fistula.

In a subsequent address, the Hunterian Oration delivered in February, 1917, Makins⁶ went further in his conclusions as to the application of venous occlusion as a therapeutic measure. In this address he advocated the possible value of ligature of the vein as a therapeutic measure in instances in which there is arterial occlusion but no fistulous opening between the artery and the vein. It is interesting, however, to note that in this address, Makins referred to the observations of von Oppel concerning the beneficial effects of simple ligation of the vein in instances of spontaneous arterial occlusion without arteriovenous fistula.

During the World War, this subject was made the principal point of discussion at a meeting of the French Surgical Society in July, 1917, at which time Professor Tuffier⁷ expressed his views on the subject in the following words:⁸

We all know that the three arterial ligations which most often expose patients to grave dangers of disturbance are (1) those of the femoral trunk, (2) those of the carotid at its bifurcation, and (3) those of the popliteal artery in the lower half of the popliteal space. If I believe everything that I have seen of ligation since the beginning of this war, it is that the occlusion of the popliteal in its lower half causes most disasters; gangrene of the limb is very often a consequence of it.

To lessen the chances of ischaemia or of the gangrene following ligatures in these regions, it has been advised to have recourse more often to lateral sutures in all cases where the nature of the lesions permitted it, and I fully share this opinion. There is a great advantage in having recourse to arterial sutures; they are less difficult to place than one believes.

5. Makins: *Gunshot Wounds of the Blood Vessels*, New York, William Wood & Company, 1919, p. 101.

6. Makins: *Lancet* 1:249, 1917.

7. Tuffier: *Bull. et mém. Soc. de chir. de Paris* 43:1469, 1917.

8. Halsted's translation.

There is a practice to which I desire again to direct your attention in this connection; it is ligation of the corresponding healthy vein in all cases of ligation of the great vessels of the root of the limbs. This question, raised long ago, can find in actual occurrences some particularly suggestive statistics. There is first a fact which appears well demonstrated; it is that ligation of the vein and of the artery in the case of wounds of the two vessels does not increase the danger of ischaemia. Moreover, the statistics of the English Army, which Sir George Makins has communicated to us, give in this connection the following ratios. Ligation of the artery alone is followed in a general way by gangrene in 40.2 per cent, whereas simultaneous ligation of the artery and of the vein under the same conditions gives 24.5 per cent; and I speak only of gangrene from ischaemia.

The most marked difference is in connection with the popliteal; ligation of the artery alone in twenty-four cases gave favorable results in 58.33 per cent, and gangrene in 41.66 per cent. Simultaneous ligation of the artery and of the vein has given in twenty-eight cases twenty-two favorable results and only six cases of gangrene.

It is interesting to note that Tuffier referred to simultaneous ligation of the vein as "a subject raised long ago." The danger of ligation of veins in the presence of suppuration was emphasized by Pirogoff. After the development of antiseptic surgery, both experimental and clinical observations were reported which justified the conclusion that ligation of the vein with the artery does not entail a risk of gangrene greater than ligation of the artery alone. I have found no record previous to the beginning of the twentieth century which contained a definite statement indicating that ligation of a vein is a therapeutic measure in the treatment of arterial disease. In a private communication, Makins stated: "At the time of the Boer War (1899-1902), I held the generally accepted view of the necessity of sparing the vein."

In a report of a study of the surgical treatment for aneurysm of the subclavian artery, Halsted⁹ discussed the subject of therapeutic occlusion of healthy veins at some length. In this publication, he called attention to the fact that occlusion of the vein, as a method of prevention of gangrene, had been recommended previous to the time of the publications of Makins. He expressed the belief that the first record of the idea is contained in a report of an operation by von Oppel,¹⁰ published in 1908. It is interesting to note that this publication of von Oppel dealt with an operation on a patient suffering from arteriovenous fistula.

It would seem, therefore, that the fundamental principles involved in therapeutic venous obstruction had been considered the same whether this operation was applied to arteriovenous fistula or to arterial obstruction without arteriovenous communication.

I believe that this opinion is erroneous and that careful study of the conditions present in varicose veins, arteriovenous fistula, and in arterial

⁹ Halsted Johns Hopkins Hosp Rep 21:1, 1921

¹⁰ Von Oppel: Arch f klin Chr 86:31, 1908.

obstruction without fistula will show that the fundamental principles involved in the application of therapeutic venous obstruction to these different conditions are not the same.

In order to make myself clear in the attempt to analyze the different conditions in the circulation of the extremities for which therapeutic venous occlusion is indicated, it will be necessary to review briefly some of the most elemental factors concerned in the circulation of blood.

In the beginning, it is worth while to point out that however complex the function of the circulation of the blood in health or the pathologic changes in blood flow in disease may be, the actual circulation of blood is only a fluid flowing through tubes. The physical and chemical characteristics of the fluid may vary and the mechanism of control of the cross-section area of the tubes may be exceedingly complex, but the fact remains that in the last analysis the circulation of the blood is a simple mechanical phenomenon.

If the circulation of the blood in health or disease is approached from this point of view, it is at once apparent that with the assumption of a constancy of the physical and chemical properties of the blood, there are two important variable factors: (1) the amount of blood which passes through a unit volume of tissue in a given time, the volume flow, and (2) the tension of the blood in the vessels through which it is passing, the intravascular pressure. It might be said that if the peripheral circulation is to be discussed from the point of view of its being a mere mechanical phenomena of a fluid flowing through tubes, volume flow was the single important factor since it is obvious that the amount of fluid which flows through a unit length of a tube is dependent on the cross-section diameter of this tube and the difference in pressures between the inflowing and outflowing points, but certain evidence exists which makes it seem likely that nutrition of the tissues is dependent on the conditions of intravascular pressure independent of volume flow. It is also worth while to emphasize another point, the lack of appreciation of which has often led to error. The volume flow of blood must, of necessity, in all instances be the summation of all the blood flowing through every channel of that particular portion of the body under consideration. For example, the cardiac output or the total amount of blood which is put out by the heart in a unit of time must be the same as that which is flowing through every capillary in the body. It is possible to have great variations in the volume flow of blood through any particular organ without necessarily changing the cardiac output or total volume flow. For example, during the process of digestion, there may be a much larger amount of blood flowing through the intra-abdominal organs and a correspondingly less amount of blood flowing through the peripheral structures. This principle is perhaps best referred to as the distribution of blood flow. The amount of blood flowing

through an extremity may be actually greater than normal, in spite of the fact that a portion of this extremity may be receiving a blood flow below that necessary for normal nutrition. I wish particularly to emphasize this point because of conclusions that are now being drawn from certain experimental work in which it is assumed that evidence of an increased volume flow of blood to a lower extremity is taken to mean that all of the tissues of this extremity are receiving an increased circulation.

The distribution of the blood flow through tissues must be considered as applying to small volumes as well as to relatively large volumes of tissue. It has been clearly demonstrated that blood may be flowing freely through a capillary at a time when no blood is flowing through another capillary a small fraction of a millimeter distant.

FUNDAMENTAL PRINCIPLES OF THERAPEUTIC VENOUS OCCLUSION

After this definition of terms, I shall proceed with a discussion of the fundamental principles involved in the application of therapeutic venous occlusion to those conditions for which it has been used.

Venous obstruction as a therapeutic measure has been applied in three conditions: varicose veins with the attendant ulceration, arteriovenous fistula and simple arterial obstruction which may be either acute complete or progressive partial.

1. In instances of varicose veins associated with poor nutrition of tissues, the condition is probably one in which the poor nutrition of the tissues is the result of an already existent venous obstruction that operates to produce a diminished volume flow of blood through some of the superficial tissues. The only reason for the occlusion of the dilated veins which has ever been assigned, paradoxical as it may seem, is the ultimate removal of this existent venous obstruction. Further discussion of this particular phase of surgery of the venous system is not appropriate at this time.

2. In instances of arteriovenous fistula, the condition is one of an abnormal communication between the artery and vein through which the blood, destined for the tissues supplied by the artery distal to the fistulous opening, is shunted directly into the vein. In this condition, there are two circulations: a normal circulation through the capillary bed of the extremity and an abnormal circulation through the fistulous track. The arteries, capillaries and veins of the extremity are presumably normal. The anatomic defect lies solely in the fistulous communication between the artery and the vein. The physiologic defect lies solely in the diminution of the volume flow through the capillary bed because part of the arterial blood passes directly into the veins through the fistulous opening. From this, it is obvious that any therapeutic

measure must have as its prime object the diversion of the volume flow of blood of the abnormal circulation into the paths of the normal circulation.

3. In instances of simple arterial occlusion without arteriovenous fistula and without any demonstrable disease of the veins, the condition is one of a reduction of inflow of blood into the arterial tree distal to

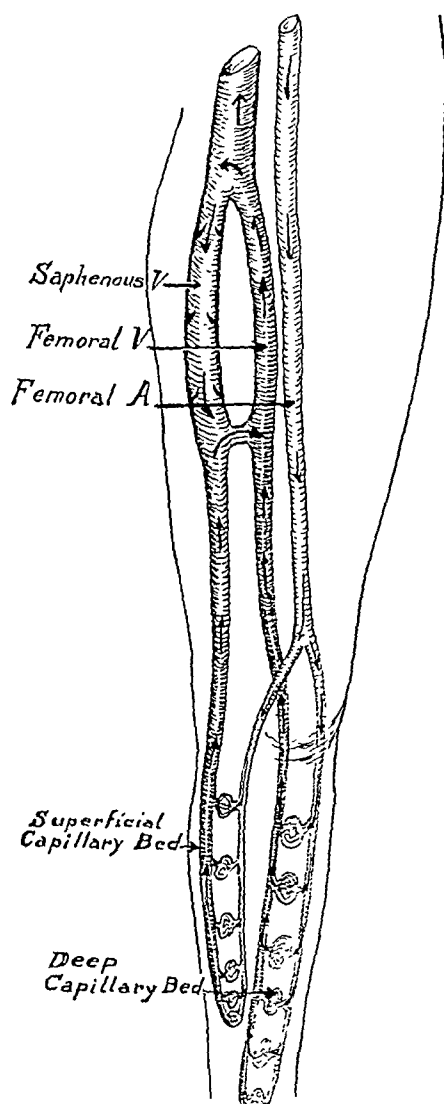


Fig. 1.—Conditions of the circulation of the extremity in the presence of varicose veins of the leg. The hydrostatic pressure in the absence of valves in the saphenous vein results in an increase in the venous pressure in the superficial veins. There is, therefore, a disproportion between the resistance offered in the capillaries of the superficial circulation and the capillaries of the deeper circulation. In this figure and figures 2, 3, 5, 6, 7, 8 and 9, *V* indicates vein and *A*, artery.

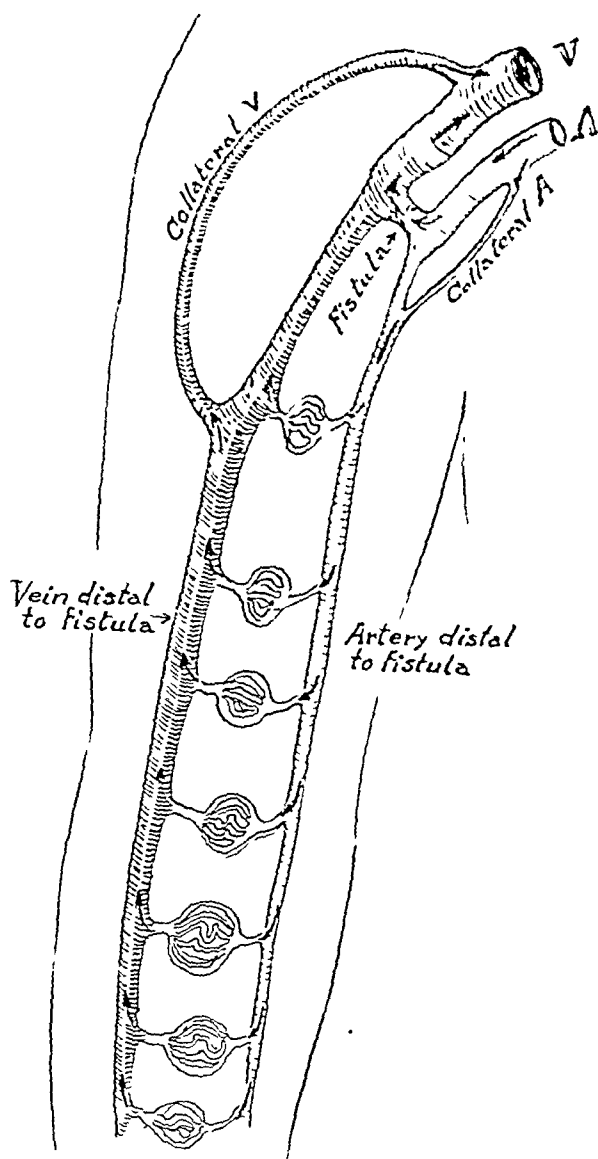


Fig. 2.—Conditions in the circulation of the arm with a fistulous opening between the axillary vein and artery. Blood may pass from the artery to the vein either through the capillaries of the arm or through the arteriovenous fistula. If the artery is obstructed just proximal to the fistulous opening, blood passing through the collateral arterial branch may also pass through the capillaries or the fistulous opening. Obstruction of the artery, therefore, merely results in a diminution in the volume flow through both circulations. The reduction of the volume flow through the capillary bed is probably in all instances proportionately greater than the reduction of the volume flow through the fistulous opening. Simultaneous ligation of the vein at the same level may diminish the volume flow of blood through the fistulous opening and increase the volume flow through the capillary bed. See also figures 4 and 9.

the point of obstruction without a corresponding reduction in the capacity of the outflow channels. There is no communication between the artery and vein other than through the capillary bed, and blood may flow from the artery to the vein through this capillary bed in all portions of the extremity. With an appreciation of the elementary principles of the flow of fluids through tubes, it becomes obvious that

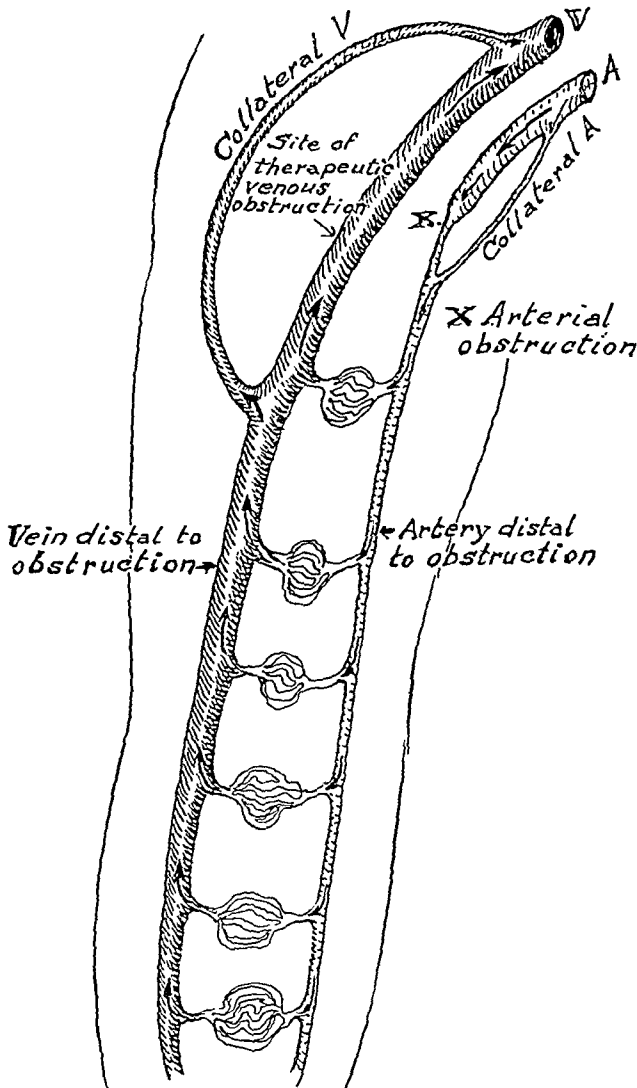


Fig. 3.—Conditions present in the circulation of the arm with simple arterial obstruction without arteriovenous fistula. No communication exists between the artery and vein except through the capillaries of the extremity. Therapeutic occlusion of the axillary vein makes it necessary for the return flow of blood to pass through the collateral vein. A difference of opinion exists as to the effects of the obstruction of the vein on the volume flow of blood through the capillaries. See also figure 7.

such a condition is of necessity associated with a diminution of volume flow through the tissues supplied by the obstructed artery and a diminished intravascular tension in the arteries, capillaries and veins. An artery may be completely obstructed suddenly by wound, ligature or embolus, or arterial obstruction may be the result of a progressive obliterating arterial disease.

It is primarily my purpose in this paper to inquire into the history of the development of the idea of therapeutic venous obstruction for arterial disease, to discuss the fundamental principles involved and to comment on the clinical applications. As has already been stated, the origin of the idea of purposeful obstruction of a healthy vein for its possible beneficial effects in instances of dangerous anemia from arterial occlusion has been attributed to experiences with arteriovenous fistula. The first advancement of this idea is usually attributed to Sir George Makins. I am convinced, however, that the idea had previously occurred to others. From a study of the literature, it seems that Makins did not clearly enunciate this idea until the delivery of his Hunterian Oration before the Royal College of Surgeons of England on Feb. 14, 1917,¹¹ and it is interesting that even at this time Makins included the evidence derived from the operative treatment of arteriovenous fistula as substantiating the conclusion that ligature of a healthy vein is to be recommended in instances of simple arterial obstruction. It is to the credit of Makins, however, that he apparently realized that ligature of the vein in arteriovenous fistula involved somewhat different principles, because he stated in his Hunterian Oration, "Evidence, moreover, exists that under certain conditions ligature of both artery and vein is a preferable procedure. The first example, *not an unmixed or simple one*,¹¹ may be sought in the results observed to follow the application of a single proximal ligature to the artery in cases of arteriovenous aneurysm.

"A more striking example is offered by the ligaturing of the popliteal vein alone for the treatment of senile gangrene of the foot by W. A. Oppel."

It is interesting that Halsted, also, apparently confused the principles underlying occlusion of the vein in the treatment for arteriovenous fistula with the principles underlying the therapeutic occlusion of the vein in instances of arterial obstruction without arteriovenous fistula.

The experience of von Oppel, to which Halsted ascribed the origin of the idea of ligation of the concomitant healthy vein in the presence of arterial obstruction, was briefly as follows:

A man, aged 32, presented the clinical manifestations of a fistula between the axillary artery and vein due to a gunshot wound. Three operations were performed on May 5, 1905. During the course of the operations, frequent observations of the blood pressure were made by Korotkow.

11. Author's italics.

The first operation was completed at 11:30 a. m., and consisted of a double ligation and division of the axillary artery proximal to the aneurysm sac. Following this procedure, the arm became deathly pale and the blood pressure, zero.

The second operation was begun at 3:30 p. m., and finished at 4:30 p. m. The wound was opened. The axillary vein was divided above the aneurysm between ligatures. No change in the arm was noted by Korotkow. The operator then observed that pressure with the finger in the space between the stumps of the divided artery caused the arm to become red and the blood pressure to rise to 40 mm. A search was then made in the vicinity in which the pressure was exerted, and a large vein (v. axilaris profunda) was found. This vein was doubly ligated and divided. The blood pressure in the arm rose to 40 mm. The wound was then closed. When the dressings were applied, it was noted that the arm was getting pale. After the patient was returned to bed, the arm continued to be pale and severe pain developed.

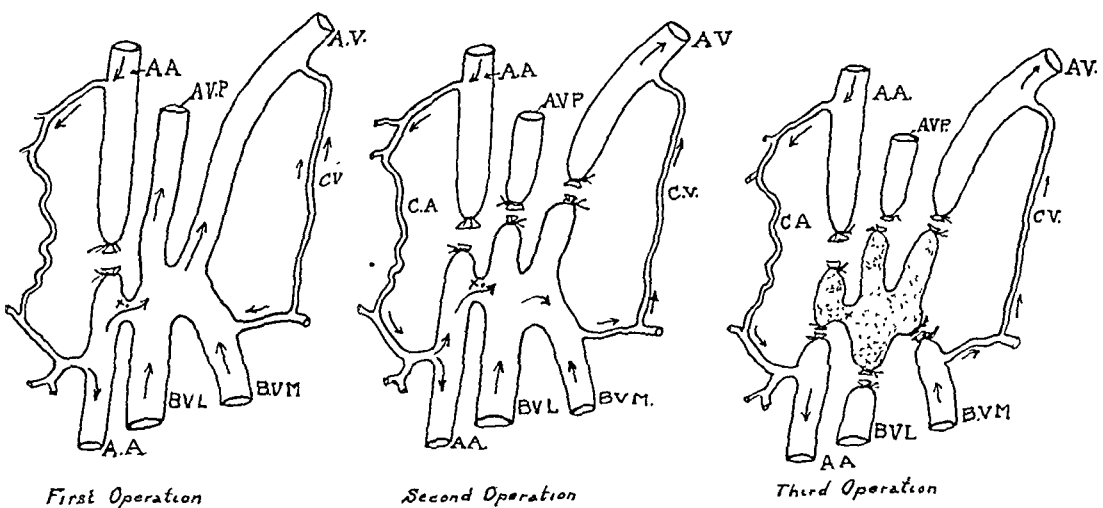


Fig. 4.—The operative procedure of von Oppel to which Halsted ascribed the origin of the idea of therapeutic ligation of the vein for prevention of gangrene. The diagrams are made from von Oppel's description. A.A., axillary artery; X., arteriovenous fistula; A.V., axillary vein; A.V.P., deep axillary vein; B.V.L., lateral brachial vein; B.V.M., medial brachial vein; C.V., collateral vein circulation; C.A., collateral arterial circulation. A description is given in the text.

The third operation was begun at 8:30 p. m., and consisted in a complete extirpation of the arteriovenous fistula. Immediately after isolation of the aneurysm sac, the arm became hyperemic and remained so for a period of twenty-four hours. Pain ceased, and an uneventful convalescence ensued.

I believe that von Oppel was in error in attributing the temporary improvement in the circulation of the arm observed during the course of the second operation to occlusion of the deep axillary vein. It would seem more likely that the pressure of the finger or the operative maneuvers of exposure of the vein resulted in temporary compression of the fistulous tract. I believe that he was also in error in his statement that the patient's condition was improved by the second operation.

The extreme pain which was present between the second and third operations would seem contradictory to this view.

This paper of von Oppel is an admirable record of the principles involved in the treatment for arteriovenous fistula. I am certain that any one who carefully reads this publication of von Oppel will be convinced that Korotkow, who was associated with von Oppel, had a clear conception of the principles involved in the ligation of the vein as a part of the operative procedure in the treatment for arteriovenous fistula. I believe that von Oppel had in mind only the conditions peculiar to arteriovenous fistula when he stated:

So far as I know, up to the present time, there has been no mention of a rôle being played by the veins in relation to the origin of gangrene of the extremities.

Von Oppel's conception of the relationship of venous obstruction to the conditions associated with arteriovenous fistula is more clearly expressed in the following statement:

When it is realized that the function of the collateral arterial circulation can be and is disturbed by the veins which suck arterial blood through the aneurysmal sac, then it is easy to draw the conclusion that those operative procedures should be chosen which will remove the aspirating effect of the veins upon the arterial blood, in other words, that procedure will be correct which, in the region of the aneurysm, *separates the bed of the arterial blood from that of the venous blood.*¹²

In the separation of the bed of the arterial blood from that of the venous lies the principle of safe operative treatment of arteriovenous aneurysm of the peripheral vessels.

I believe that the first appreciation of the fundamental principles underlying therapeutic venous occlusion for arterial obstruction without arteriovenous fistula is to be found in the records of the experiences with an operative procedure opposite in nature to the operative method applicable to arteriovenous fistula.

In 1902, Carrel and Morrel attempted some experiments, the object of which was the reversal of the circulation in an extremity. During the same year, both Satrustegui¹² and Jaboulay attempted to produce a fistulous opening between the femoral artery and the femoral vein with the idea that this procedure would be beneficial in patients in whom gangrene of the extremity seemed imminent. In 1906, Carrel¹³ showed conclusively that reversal of the circulation was possible in the experimental animal. In the same year, Hubbard¹⁴ of Boston and Lilienthal¹⁵ of New York reported instances of the application of this operative procedure for the treatment of impending gangrene of an extremity.

12. Satrustegui: Bull. med., Madrid, 1902.

13. Carrel and Guthrie: Ann. Surg. 43:203, 1906.

14. Hubbard: Ann. Surg. 44:559, 1906.

15. Lilienthal: Ann. Surg. 45:1, 1907.

In 1908, Wieting¹⁶ of Constantinople described the indications, the operative technic and the results of an operation intended to reverse the circulation in the arteries and veins of an extremity in instances of arterial occlusion. In spite of the priority of the publications of Carrel, Hubbard and Lilienthal, this operation is still referred to in the literature as the Wieting operation. Following Wieting's report, there was much discussion as to the value of this operation as a therapeutic measure and as to the possibility of its actually resulting in a reversal of the direction of blood flow through the capillaries. The controversy between Wieting and Coenen¹⁷ was particularly spirited. Wieting enthusiastically contended for the success of the operative procedure and discredited all experimental work which led to conclusions contrary to his own. The result of the controversy was the stimulation of a wider interest in the problems concerned.

The technic of the operative procedure which stimulated so much interest in the surgical treatment for diseases of the circulation of the extremities was variously modified. The original procedure consisted in a complete division of both the artery and the vein, transposition of the stumps of the vessels and end-to-end sutures. The operative technic was changed to one in which the vein was ligated, the artery divided, the distal stump of the artery ligated, and an anastomosis made between the proximal arterial stump and the vein distal to the ligation. The same result was accomplished by another modification of the operative technic, in which a lateral anastomosis of the artery and vein was made and the vein ligated proximal to and the artery distal to the fistulous opening. The final modification of the operation consisted of a lateral anastomosis of artery and vein and ligation of the vein proximal to artificial arteriovenous fistula.

The result of the interest in these operative procedures was the stimulation of a considerable amount of experimental work, of which some of the most interesting and valuable contributions have been overlooked because of their publication in the Russian language. It would seem, however, that von Oppel and his assistants were the first to call attention to the possibility that all the beneficial results which had followed the various operative procedures for reversal of the circulation had been due to venous obstruction rather than actual reversal of the circulation. Von Oppel, therefore, advanced the idea that the logical procedure in instances of arterial obstruction was the ligation of the vein. As evidence of the truth of this, he¹⁸ reported in 1913 six instances of marked anemia of the lower extremity in which definite evidences of improvement had followed ligation of the popliteal vein.

16. Wieting: *Deutsche med. Wchnschr.* **34**:1215, 1908.

17. Coenen: *Zentralbl. f. Chir.* **38**:106, 1911.

18. Von Oppel: *Vrach. Gaz.* **20**:303, 1913.

It is to this report that Makins referred in his Hunterian Oration in which he first advocated the ligation of the vein in instances of arterial obstruction without arteriovenous fistula.

It would seem, therefore, as if the idea of therapeutic venous occlusion for simple arterial obstruction grew out of the experiences with an operative procedure which in reality is a procedure quite opposite to that usually considered the origin of the idea.

In passing it may be said that no better evidence of the lack of knowledge of the elementary principles of the circulation of blood could be cited than the fact that a condition recognized as the cause of gangrene

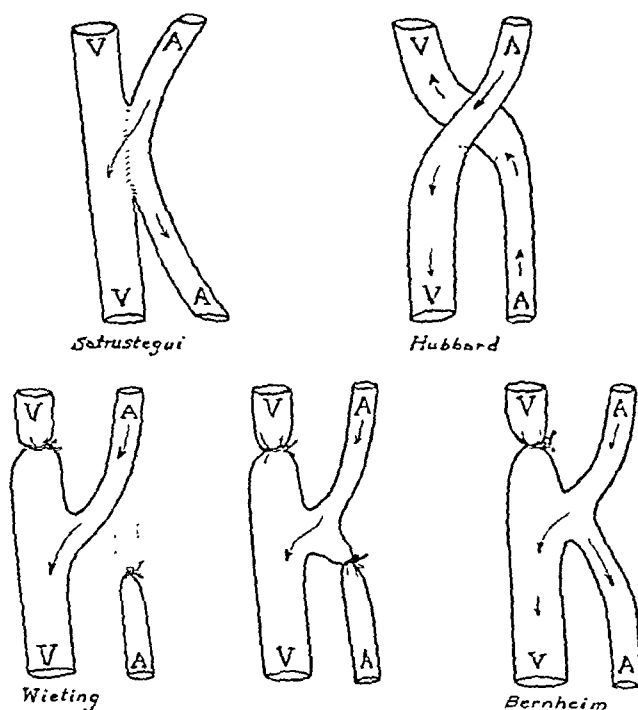


Fig. 5.—The various modifications of the operative procedure designed to reverse the circulation of an extremity.

was produced as a means of its relief. It is also worth while to call attention to the fact that during this period of awakened interest in therapeutic venous occlusion, there was apparently no clearcut definition of the different conditions to which it was deemed applicable. Von Oppel revealed his conception of the abnormal conditions of the circulation due to arterial obstruction when he wrote:¹⁹

As is known, angiosclerotic gangrene begins because of the lack of arterial blood supply. In instances of diminished circulation of an extremity, if the extremity is elevated, it becomes deathly pale and the characteristic ischemic pain

19. Translated from the Russian by Mr. Myer Epstein, Vanderbilt University Medical School and abstracted by the author.

ensues. If the extremity is then put into dependent position, hyperemia appears and the pain disappears. Why is this so? Observation of the blood pressure in the thigh in a patient with impending gangrene shows the blood pressure to be 30-50 mm. of mercury, which is about that of collateral arterial pressure after occlusion of the major arterial trunk. The blood pressure is, therefore, sufficiently low so that the hydrostatic pressure from the horizontal position is enough to cause cessation of the circulation. Maniewsky's experiments show that the Trendelenburg position may cause the pressure in the femoral vein to diminish nearly to zero. This is true if the arteries are healthy and the extremity is comparatively short. It is clear that with a diminished inflow of blood, this phenomenon would be exaggerated. Diminution in the venous pressure will result in a sucking into the vein of the collateral arterial blood supply and thus divert it from reaching the more distal aspects of the extremity. When the extremity is placed in the dependent position the weight of the blood in the arterial tree will be sufficient to cause a dilatation of the arteries, and the venous pressure will be increased. The advantage of the dependent position in preserving the nutrition of the tissues in patients with incipient gangrene is shown by the fact that these patients always prefer the extremity to be in the dependent position. In some instances, the patient cannot even endure the horizontal position. Both clinical and experimental observations show that ligation of the vein is associated with an increase in the pressure in the veins and arteries.

On these observations, I have recommended the ligation of the vein as a palliative procedure in instances of ischemic conditions, realizing that this procedure produces a reduction²⁰ in the circulation but is beneficial to the patient, at least for a time, in preventing the pain and helping to limit the gangrene. Ligation of the vein is beneficial not because the outflow is reduced, but because reduction in the outflow favorably influences the arterial circulation.

EXPERIMENTAL WORK

It would be impossible to review all the experimental work which has a bearing on therapeutic venous obstruction. Many important observations bearing on this subject are contained in the records of researches, the purpose of which was the study of other problems in the circulation. A brief review of a few of the most recent publications, devoted exclusively to the simultaneous ligation of the vein as a therapeutic measure in arterial obstruction, is sufficient for the object of this paper.

At the Conference of Inter-Allied Surgeons in Paris in 1917, van Kend²¹ reported some experimental work, the conclusions of which were reported by Makins as follows:

In carrying out a series of experiments made with the object of determining the indications and physiological basis for transfusion of blood, I have had the opportunity of measuring the blood pressure in limbs of which the main artery had been ligatured. The blood pressure was taken successively after the artery alone had been tied and again when ligature of the vein had been superadded.

20. In "reduction of the circulation," I believe that von Oppel had in mind the entire extremity and not its most peripheral aspects.

21. Van Kend: *Compt. rend. conf. chir. internat.*, Paris, 1917, p. 348.

My observations confirm the view that has been expressed by Sir George Makins. In fact, plethysmographic tracings demonstrate clearly that a slight rise in the blood pressure in the limb follows the application of a ligature to a main vein after previous ligature of the artery. It appears then from the standpoint of the physiologist that to leave the main vein viable after occlusion of the main artery of a limb diminishes what may be called the residuary blood pressure maintained by the collateral circulation. If the contribution of the collateral circulation is allowed to remain with the main vein intact it is natural that the residuary blood pressure should fall. If this view be adopted, ligature of the vein as well as the artery should be recommended in order to retain the blood supplied in longer contact with the tissues. Thus the most satisfactory conditions for the maintenance of the nutrition of the organs are provided, because the obstacle to the return circulation provided by the ligature retains the blood for a longer period in the member.

Makins also quoted from a private communication received from Major Hamilton Drummond in which Drummond reported having found, from experiments made on loops of intestine of the cat, that gangrene more frequently followed ligation of the arteries alone than if both the arteries and the veins were obstructed.

The only experimental work which Halsted reported in his discussion of therapeutic venous occlusion for the relief of symptoms following arterial occlusion is the result of six experiments in which the blood pressure in the arteries distal to the arterial occlusion was measured before and after occlusion of the concomitant vein. It was found that venous obstruction was always followed by an increase in the intra-arterial tension and that release of the venous occlusion was followed by a diminution in the intra-arterial pressure.

Experimental work which was undertaken for the study of other physiologic changes than those of blood pressure was reported by Brooks and Martin²² in 1923. In these experiments, it was found that the blood pressure in the artery distal to the point of occlusion was increased by the occlusion of the vein at the level of arterial occlusion. The pressure in the vein distal to the point of occlusion was increased relatively more than the pressure in the artery. The effect of the venous obstruction on the volume flow of blood in the tissues was studied by means of determinations of temperature in the tissue. It was found that after occlusion of the artery the temperature of the tissues, supplied by this vessel, was diminished and that further diminution occurred if the concomitant vein was also obstructed. From these facts, it was concluded that in instances of arterial obstruction occlusion of the concomitant vein resulted in an increase in intravascular blood pressure of all the vessels distal to the occlusions, and that the diminution of the

22. Brooks, B., and Martin, K. A.: Simultaneous Ligation of Vein and Artery. *J. A. M. A.* 80:1678 (June 9) 1923.

volume flow of blood which resulted from the arterial occlusion was further diminished by the venous obstruction.

The effect of ligation of the concomitant vein on the incidence of gangrene in arterial obstruction was studied in a comparatively large series of experimental animals. It was found that the incidence of gangrene was decidedly less in those instances of obstruction of both artery and vein than in those instances in which the artery alone was obstructed.

From these experiments it was concluded that obstruction of the concomitant vein in the presence of arterial obstruction resulted in an increase in intravascular pressure but in a decrease in volume flow of blood through the tissues. The diminished incidence of gangrene, in spite of the diminished volume flow of blood, was attributed to the beneficial effects of the increased intravascular tension which probably operated in such a way as to produce a more equitable distribution of the blood flow.

More recent experimental work by Holman²³ and by Theis²⁴ has confirmed the effects of concomitant ligation of the vein on the blood pressure, but both Holman and Theis have reached a conclusion contradictory to that of Brooks and Martin concerning the effect of concomitant venous obstruction on the volume flow of blood. I believe that both of these investigators are in error in that they have not correctly interpreted their experimental observations. Both of these investigators have used the same method for estimating the effects of obstruction of the vein on the volume flow of blood. This method consists in observing the flow of blood from a cannula placed in the artery distal to the point of arterial obstruction. It was found that the amount of blood which flowed out through the cannula was increased if the vein was obstructed. This fact was interpreted by both of these investigators to indicate an increase in volume flow of blood through the tissues after occlusion of the vein. It would seem obvious that the increased flow of blood from the cannula in the artery distal to the obstruction would be the result of an obstruction to the outflow of blood and the corresponding increase in intravascular pressure and would thus be an evidence of diminished rather than increased volume flow through the tissues.

Other physiologic changes resulting from intentional occlusion of veins have been studied experimentally. Holman and Edwards, from experiments on dogs, found that the arterial blood pressure distal to the point of arterial obstruction was increased relatively more if the vein

23. Holman, E., and Edwards, M. E.: *New Principle in Surgery of Large Vessels*, J. A. M. A. **88**:909 (March 19) 1927.

24. Theis, F. V.: *Ligature of Artery and Concomitant Vein in Operation on Large Blood Vessels*, Arch. Surg. **17**:244 (Aug.) 1928.

was occluded at a level nearer the heart than at the site of the arterial obstruction. These investigators believed that the occlusion of the vein at this relatively higher level caused an increase in the peripheral resistance of the circulatory bed supplied by the arteries furnishing the collateral branches, and thus caused a diversion of blood through the collateral paths of circulation into the arterial system distal to the point

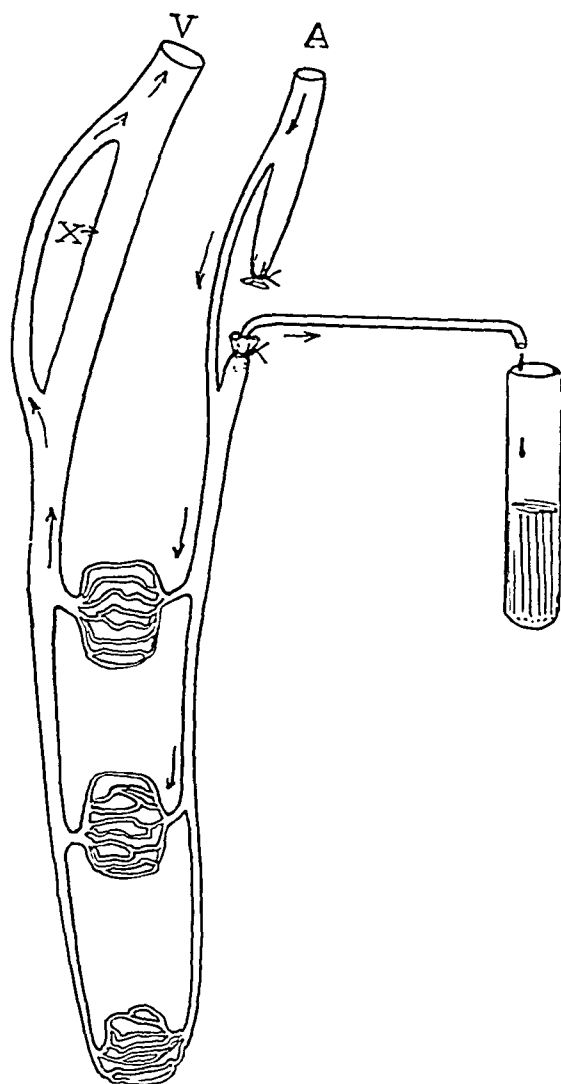


Fig. 6.—The experimental method used by Holman to determine the effects of ligation of the vein on the volume flow of blood through an extremity. It is obvious that obstruction of the vein at *X* would result in more blood flowing through the cannula. The fact that more blood flows from the cannula is not an indication of an increased volume flow of blood through the capillaries, but is evidence for the truth of the contrary conclusion.

of arterial obstruction. This conclusion is based on the fact that ligation of the vein at a higher level causes more increase in the intra-arterial pressure distal to the arterial occlusion than ligation of the

vein at the same level of arterial occlusion. This possibility was also considered by Brooks and Martin, but no experimental evidence could be found to substantiate it. As a matter of fact, their observations were such as to lead them to believe that this diversion of blood flow did not actually occur.

The effects of venous occlusion on the number and size of the paths of collateral arterial circulation about a site of arterial obstruction have been studied experimentally by Pearse²⁵ and by Theis.²⁴ Pearse found that ligation of the artery and vein was always followed by a richer collateral vascular bed than that following obstruction of the artery alone. On the other hand, Theis found that the collateral circulatory bed was better developed in those instances in which the artery and vein were occluded only if the determination was made immediately after the experimental vascular occlusion. In observations on the experimental animals, after a period of three weeks, the vascular bed was richer in those instances in which the artery alone was occluded.

The different results obtained by these investigators must have been due to a difference in the experimental methods used. It is worth while, however, to call attention to the fact that the size of blood vessels as determined by injection is not a reliable index of the actual volume flow of blood through tissues, and also to the fact that the condition of the circulatory bed three weeks after a sudden arterial occlusion is not necessarily important in the study of the cause of gangrene.

The conclusions from all observations concerning the physiologic effects of obstruction of a vein in the presence of arterial obstruction may then be briefly summarized as follows:

1. All observers agree that ligation of the concomitant vein in the presence of simple arterial obstruction is followed by an increase in the blood pressure in both the veins and the arteries distal to the level of obstruction.

2. Both experimental and clinical experience indicate that the incidence of gangrene is diminished.

3. In the attempts to explain the beneficial effects of therapeutic venous obstruction on the manifestations of arterial occlusion without arteriovenous fistula is found the confusion of ideas. Some are content to assign the beneficial effects to the "retention of blood in the tissues" or to a "restoration of the balance in circulation." With a clear conception of the fundamental principles of circulation of blood and the specific conditions under consideration, it becomes evident that the important differences of opinion, in regard to the effects of therapeutic venous obstruction, lie in the different views held concerning the influence of this procedure on the distribution of the volume flow of blood.

25. Pearse: *Ann. Surg.* 86:850, 1927.

It would seem as if all observers, except Brooks and Martin, believed that ligation of the vein was beneficial because this procedure increased the volume flow of blood in the capillary bed of the distal aspect of the extremity. If such is true, then the fundamental principles involved may be the same in therapeutic venous obstruction whether it is applied as treatment for arteriovenous fistula or for simple arterial obstruction.

If the conclusions drawn from the experiments reported by Brooks and Martin and other unpublished experiments of mine are true, the beneficial results of therapeutic venous occlusion in instances of simple arterial occlusion are not because blood flow is increased in the distal aspects of the extremity, but because the blood flowing through the distal aspect of the extremity is more equably distributed in the capillaries and is under greater tension in all the vessels. The actual amount

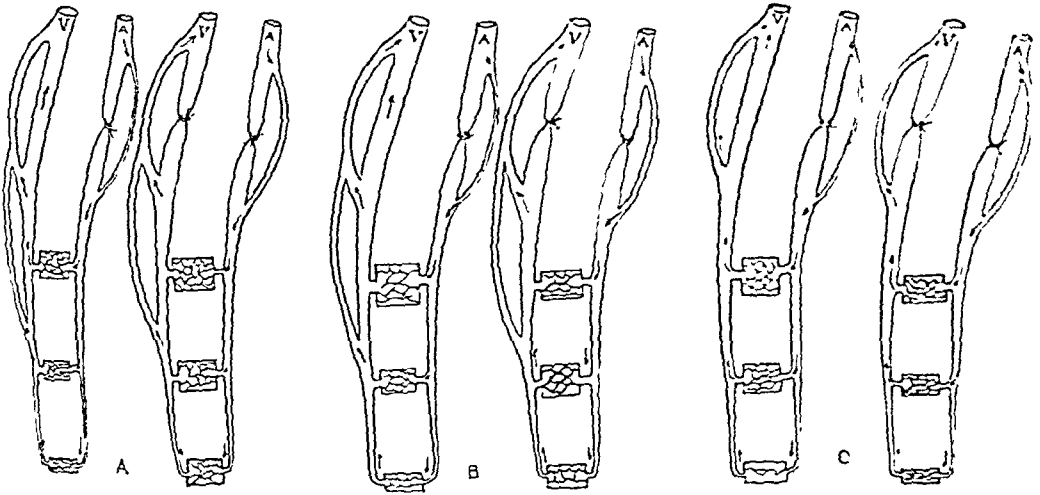


Fig. 7.—The different ideas which have been expressed as to the effect of simultaneous ligation of the vein on the volume flow of blood. In these diagrams the amount of the volume flow of blood in the capillary beds of the different aspects of the extremity is indicated by the vertical height of the rectangles. The distribution of the blood in the capillaries is indicated by the network in the rectangular spaces. The intracapillary pressure is indicated by the relative thickness of the lines of the network. In *A* it will be seen that ligation of the vein is followed by an increase in the amount of volume flow and intracapillary pressure in all aspects of the extremity. In *B* ligation of the vein is followed by a diminution in the volume flow through the proximal aspect of the extremity and an increase in the volume flow through the distal aspects of the extremity. The intracapillary pressure is increased in all aspects, and no change is indicated in the distribution of the flow in the capillaries. In *C* it will be noted that the volume flow of blood is diminished in all aspects of the extremity after ligation of the vein. The intracapillary pressure is increased in all parts. The distribution of the flow in the capillaries of the most distal aspect of the extremity before ligation of the vein is irregular, while after ligation of the vein it is homogeneous.

of the blood flowing through the distal tissues of the extremity is diminished by ligation of the vein. The principles involved in this view are entirely different from those concerned in therapeutic venous occlusion in the presence of arteriovenous fistula.

From a consideration of these facts, it would seem as if any existent difference of opinion was a matter of only academic interest, and that from the purely practical point of view the indications for therapeutic venous obstruction are clearly defined. Such is not the case. The conditions so far discussed have been considered from the point of view of their being fixed or unchanging. In the clinical application of the principles of therapeutic venous occlusion for arterial obstruction, it must be borne in mind that the situation is made more complex because the conditions are constantly changing and thus the remote

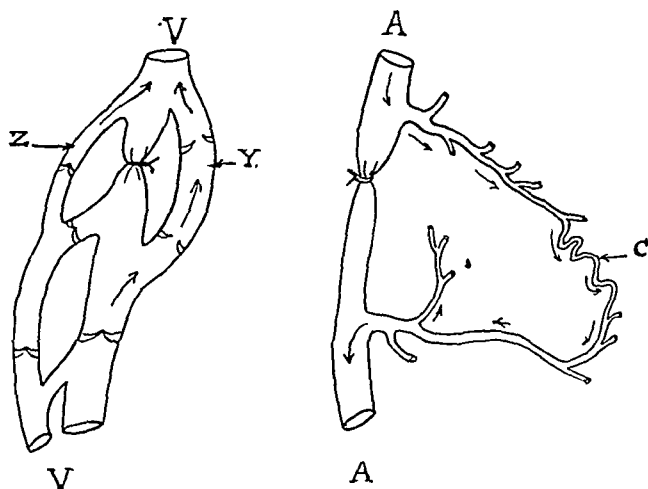


Fig. 8.—The differences in the conditions attending the development of collateral circulation in arteries (*A*) and in veins (*V*). It will be noted in *A* that the collateral circulation is from a branch proximal to the arterial obstruction through the collateral anastomotic branch (*C*) and thence in the reversed direction through the artery forming the distal aspect of the collateral arch. It is obvious that the amount of blood which passes through the collateral arch may continue to increase with an increase in the cross-section area of the arch. In *V* it will be noted that the collateral circulation about the obstruction is prevented from developing through the channel *Z* on account of the action of the valves. If it develops through the channel *Y* and this vessel subsequently enlarges, then its valves become incompetent.

as well as the immediate effects must be considered. In sudden arterial obstruction, from a wound or embolus, the greatest interference with the blood supply is immediate and without further complications, the blood flow through the anemic tissues may be expected to increase with the development of the collateral circulation. In instances of chronic arterial obstruction due to progressive obliterative arterial disease, there

may be a constant or intermittent change in the opposite direction. Also the amount of venous obstruction which is produced by the ligature of a vein does not remain fixed. Paths of collateral circulation develop about points of venous obstruction. Important differences exist between development of collateral circulation in veins and in arteries.

The sole source of energy for the propulsion of the blood stream through the arteries is the contraction of the heart. The development of collateral circulation about a point of arterial obstruction is necessarily associated with a reversal of the direction of flow through the artery constituting the distal aspect of the collateral arch.

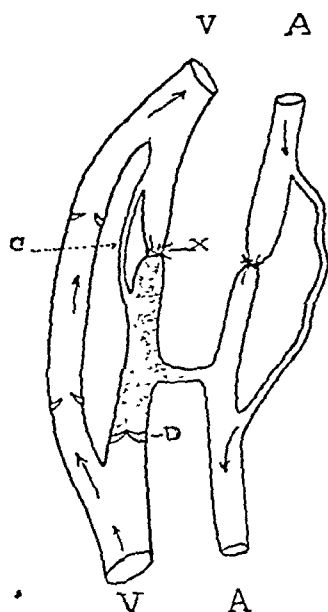


Fig. 9.—The effect of simultaneous ligation of the vein in the presence of arteriovenous fistula. In the conditions represented in the diagram, it will be seen that with ligation of the vein at *X* with the competence of the valve at *D* only such blood can pass through the fistula as could return to the heart through the vein (*C*). This would be true only if the pressure within the dotted area was insufficient to cause a breaking down of the valve at *D*. Subsequent increase in the pressure in the dotted area or dilatation of the vein at *D* would open new channels for the return flow of blood passing through the fistulous opening. This diagram illustrates a principle which may explain the temporary "improvement" sometimes observed in the treatment of arteriovenous fistula by simple proximal ligation of artery and vein. This condition may have been present immediately after the second operation in von Oppel's case.

The capacity of the collateral arterial circulation is therefore determined solely by the cross-section area of the collateral anastomotic branches.

The energy for propulsion of the blood through the veins is derived from three sources: 1. Diastole of the right side of the heart aspirates

blood from the adjacent large veins. 2. The blood may also be propelled through veins by the force of the left side of the heart transmitted through the arteries and capillaries. 3. In veins with valves, the flow of blood is accelerated by the alternate compression and relaxation of the vein by motion of the adjacent tissues. The operation of this factor is dependent on the fact that the valves in the vein permit the flow of blood in only one direction. The last factor is of great importance in propelling blood through veins of the extremity.

If collateral circulation in veins is considered in the light of these facts, it is obvious that a venous collateral circulation cannot develop by the reversal of the direction of the current through veins with competent valves. Furthermore, if the collateral circulation is through veins in the normal direction, then dilatation of these veins renders the valves inefficient.

These statements are in accord with clinical experience. If an extremity successfully passes through the immediate critical stage following simple arterial occlusion, a satisfactory permanent recovery may be anticipated. If, however, the manifestations of severe venous obstruction develop, convalescence is prolonged and often never complete.

It would seem, therefore, as if the remote effects of therapeutic venous obstruction must be taken into consideration. In other words, ligation of a vein might be the means of averting gangrene but the cause of subsequent chronic venous stasis. The clinical experience available is not sufficient for drawing definite conclusions. A letter from Sir George Makins, written in May, 1922, stated:

I have seen some swollen extremities and varicose veins amongst the war pensioners, but in all the cases I have had the opportunity of examining, the injury to the vessels was accompanied either by very extensive wounds with loss of substance, or fracture of the femur or pelvis. I have not been able to regard these cases as a fair test, and no uncomplicated case of ligation of artery and vein with unsatisfactory after consequences has come under my notice.

Still, I think the question of the ultimate condition of the limb must be considered undecided.

My own clinical experience leads me to believe that venous occlusion of an amount sufficient to be of value in the prevention of gangrene is often followed by manifestations of venous stasis from which convalescence is prolonged or incomplete.

From a consideration of all evidence available, I believe that the following statements are substantiated by the results of experimental study and clinical experience.

A. In operations for the cure of arteriovenous fistula, the vein should always be ligated in any of the following conditions: (a) If in the course of an operation the artery has already been ligated and

it is then found that the complexity of the condition present makes it seem beyond the skill of the operator to attempt to close the fistulous opening, or if the surgeon is uncertain of the success of his attempts, then ligation of the vein proximal to the fistula is imperative (fig. 9a). (b) If an arteriovenous fistula has existed for a relatively short period and if it is necessary to obliterate the artery in order to close the fistula, then ligation of the vein is preferable in most instances and is always indicated if the artery is either the popliteal or the axillary. If an arteriovenous fistula is of long duration, the collateral arterial circulation is so abundant that even though it is necessary to obliterate the main artery in closing the fistula, ligation of the vein is unnecessary and even contraindicated. (c) There is a certain amount of justification in the view that ligation of the vein is always preferable in the treatment for arteriovenous fistula because of the danger of pulmonary embolism from thrombosis at the site of repair of the fistulous opening in the vein. I do not subscribe to this view.

B. In progressive arterial degenerative disease, associated with arterial obstruction, ligation of the vein is at most a palliative measure, the beneficial effects of which only occasionally justify its employment.

C. In instances of sudden arterial occlusion, therapeutic venous obstruction finds its most valuable applications.

If from traumatism or in the course of any operation it becomes necessary to ligate a large artery, simultaneous ligation of the concomitant vein should always be considered. If the artery ligated is the popliteal or axillary, I believe that ligation of the like named vein is definitely indicated. In instances of ligation of the femoral or brachial arteries, I am inclined to believe that simultaneous ligation of the vein in reality makes little or no difference. If the common femoral artery is ligated, I am inclined to believe that it is wiser to close the wound without ligating the vein, to watch the extremity carefully for signs of impending gangrene, and to ligate the vein only after such signs are evident. From my own experience, I believe that ligation of the common iliac artery is not an indication for ligation of the common iliac vein.

CONCLUSION

Simultaneous ligation of the vein is not to be considered the preferable procedure in all arterial ligations. It is to be applied only in those instances in which without ligation of the vein gangrene would be expected. In these instances, the probable immediate beneficial effects in preventing gangrene must be balanced with the possible remote ill effects of chronic venous stasis.

THE STRUCTURE OF BONE

WITH PARTICULAR REFERENCE TO ITS FIBRILLAR NATURE
AND THE RELATION OF FUNCTION TO INTERNAL
ARCHITECTURE *

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CONTENTS

Coarse-Fibered or Primary Bone	
Fine-Fibered or Lamellar Bone	
General Structure of Lamellar Bone	
The Compacta	
The Canals	
Haversian Systems	
Bone Cells	
The Fibrillar Structure of the Haversian Lamellae	
The Ground Lamellae	
The Interstitial Lamellae	
The Cement Lines	
Sharpey Fibers	
Elastic Fibers	
The Spongiosa	
Origin	
Structure	
The Relation of Function to the Structure of Bone: Wolff's Law	
The Origin of the Conception of Wolff's Law	
The Law	
Objections to the Law	

The microscopic anatomy of bone has been carefully studied by the older anatomists and histologists. All the controversial points have not been settled, and many questions still remain open. However, judging from the limited knowledge of bone structure that is prevalent now, except among those especially interested in the subject, one would think that this work had not been done. Perhaps there is a correlation between the dearth of recognized pathologic exposition of bone conditions and the lack of dissemination of histo-anatomic knowledge of bone. With the development of surgery of the bones and joints in recent years, many pathologic conditions, heretofore recognized only clinically, have become available for pathologic study. This work will be done mainly by surgeons and surgical pathologists, who will obviously base their interpretations on deviations from the normal. Since no

detailed study of the structure of bone exists in American literature, it was thought that such an exposition might prove helpful to surgeons who are interested in bone as a tissue. The possibilities of improving the character of the work done on bone will be enhanced by a knowledge of the nature of the tissue.

Another reason why the study of bone is approached hesitatingly is that its histologic preparation is believed to be difficult. In another paper,¹ I have given directions for the preparation of bone for histologic study, and many of the methods could be applied to pathologic bone with great advantage.

In this paper, I am emphasizing that phase of bone structure which is least discussed. An effort is made to describe the general architecture of bone, and its fibrillar constitution is particularly emphasized. Osteoblasts have been only casually referred to, for when bone is already formed, they are structurally unimportant. The canal systems and their anastomoses have been discussed only in passing, and a description of the circulation has been omitted since it is unnecessary for an understanding of the structure of bone. The bone cells have been described in regard to their form but not in regard to function. Furthermore, these subjects are important enough to warrant special consideration.

COARSE-FIBERED OR PRIMARY BONE

Mammalian bone consists of collagen fibers and cells which are embedded in a cement substance containing calcium salts. There are essentially two types of bone, depending on the character and arrangement of the collagen fibers. In the bone which characterizes the skeleton of the human fetus and the new-born, the fibers are irregular and mainly coarse, and the cells are large, numerous and irregular. This type of bone practically disappears by the fourth year of life, and it is replaced by typical adult bone, which has for its distinguishing character fine fibers in lamellar arrangement. In different species of lower mammals the time interval, during which the coarse-fibered bone is replaced by lamellar bone, varies.

Phylogenetically, coarse-fibered bone is the older and more primitive bone tissue. Some of the lowest vertebrates retain this type of bone for their adult skeleton, and it represents the greatest part of their periosteally formed bone. Coarse-fibered bone is the type of bone generally seen in ossified fibrous tumors and in osteogenic sarcomas, and it is the first bone formed in the repair of a lesion of the bone even in the adult. In short, whenever new bone is being formed, except in the case of the normal reconstruction that goes on constantly in lamellar

1. Jaffe: Methods for the Histologic Study of Normal and Diseased Bone. Arch. Path., to be published.

bone, it is first formed as fiber bone, which may later be replaced by lamellar bone. Coarse-fibered bone persists in adult man in those places in which tendons are attached to bone and, according to Meyer, in the bony capsule of the labyrinth of the ear. Sometimes small nests of fiber bone with thick Sharpey fibers may be seen in adult cortical bone.

When bone is first formed in the fetus, either as membrane or endochondral bone, it consists of trabeculae containing coarse fibers and cells between which lies a loose, vascular, connective tissue in which the primitive marrow develops. The structure of coarse-fibered bone may be studied in older fetuses and in the new-born in which it is laid down beneath the periosteum or is deposited on the calcified cartilaginous trabeculae in endochondral ossification. If one examines a cross-section of the diaphysis of a tubular bone or the mesodermal bone of the jaw of a 6 months fetus, it shows numerous haversian canals which are only rarely circular in cross-section, being generally somewhat elongated. Wide anastomoses are often seen between them. Irregular bony trabeculae lined by osteoblasts are present between the canals. The main direction of the haversian canals is longitudinal, as it is in adults (fig. 1). Immediately about the haversian canals the bone is least dense, but the bone between two adjacent haversian canals is more dense. Here the fiber bone consists of closely meshed, interlacing and decussating fiber bundles in which numerous irregularly disposed bone cells are embedded. Most of the fibers are thick and coarse. The fiber bundles measure from 2 to 27 microns across, but average from 12 to 15 microns. The larger bundles consist of groups of smaller bundles. The bundles are separated from each other by a layer of cement substance, or by some disordered fibrils. The marked irregularity of arrangement of these fibers is as much a characteristic of this bone as the thickness of the fibers. The mass of thick decussating fibers between two haversian canals was designated by Gegenbaur² as *Wurzelstock* (fig. 2).

The coarser fibers of primary bone are better known as Sharpey fibers. While present in great numbers in the bone of the fetus and new-born, few are contained in adult bone. They were described by Sharpey in adult bone in the sixth edition of Quain's anatomy and have also been studied extensively by Mueller³ and Koelliker.⁴ Developmentally, their origin is different from that of the fine fibrils of lamellar

2. Gegenbaur: Ueber die Bildung des Knochengewebes, *Mitt. Jen. Ztschr. f. Med. u. Naturwiss.* 1:341, 1864; 3:205, 1867.

3. Mueller: Ueber Sharpey's durchbohrende Fasern im Knochen, *Wuerzburg naturwiss. Ztschr.* 1:296, 1860.

4. Koelliker: *Handbuch der Gewebelehre*, 1889, vol. 1.

bone, since they are derived from the periosteum. Von Ebner⁵ and others described them as connective tissue and collagenous fiber-, and Koelliker expressed the belief that some of them, particularly the thicker ones, may be partially calcified. In the fetus and the new-born, they are best seen in longitudinal sections of the periosteal trabeculae of tubular bones. By the fourth year, their appearance and number are the same as those in adult bone.



Fig. 1—Part of a cross-section through the diaphysis of a long bone of a 6 months fetus, showing fibrous periosteum, osteoblastic periosteum, irregular trabeculae lined by osteoblasts and large haversian spaces with primitive marrow.

Numerous anastomosing bone cells are embedded between the fiber bundles, either singly or in groups. These bone cells are larger than those of adult bone. The lacunae, therefore, are larger and somewhat irregular. The processes of the bone cells of coarse-fibered bone are shorter, thicker and fewer than those of adult bone cells, and the canaliculi are correspondingly shorter and wider. If the lacunae of

⁵ Von Ebner: Ueber den feineren Bau der Knochensubstanz. Sitzungsab. d. Akad. d. Wissensch. 71-72:49, 1875.

the bone cells are closely packed, they may fuse and produce large spaces into which parts of the fiber bundles or groups of disordered fibrils may enter. In recently formed fiber bone, the cells are more numerous and newly formed trabeculae underneath the periosteum may consist of so many cells that the bone has a fenestrated appearance. This is also true of the fiber bone removed from the neighborhood of healing fractures, examination of which will show trabeculae that consist preponderantly of irregularly dispersed bone cells, held in the meshes between matted fibers (fig. 3).

A section through a long bone of an infant in the region of endochondral ossification shows the difference in structure between the



Fig. 2.—The thick fibers of the Wurzelstock between the haversian canals. Frozen section from skull of an infant, aged 12 weeks. Bielschowsky silver stain.

primary coarse-fibered bone deposited on the calcified cartilage cores and the primary coarse-fibered bone formed by the periosteum. Primary endochondral bone is similar in fibrillar structure to the periosteal primary bone, except that, as has been observed by von Ebner, the thick centrally placed mass which was described as Wurzelstock by Gegenbaur is absent, its place being occupied by calcified cartilage cores. The line of junction between the cartilage core and bone is irregular and corresponds in many respects to the cement lines of adult bone. Otherwise, cement lines are practically absent.

In man the character of the fiber bone rapidly changes, and soon after birth a cross-section through the diaphysis of some of the bones will show that the haversian canals have narrowed considerably in

diameter, that there is a tendency for the fibers to be disposed more regularly, particularly about the canals, where the fibers are thinner, and that the bone cells near the canals appear more like the bone cells of lamellar bone. A few thick fiber bundles may course through the fibrils arranged around the haversian canal and may enter the canal.

The problem that is still controversial is the part that osteoblasts play in the formation of fiber bone. Many believe that coarse-fibered bone results from a bony transformation of mesenchymal or embryonal connective tissue, during which calcium salts are deposited between the



Fig 3—Newly formed trabeculae under the periosteum showing numerous irregularly disposed bone cells. This should be compared with figure 5.

fibers, and in the formation of which osteoblasts play no part. They believe that in the formation of this bone the connective tissue cells become transformed into bone cells. There are others who believe that the primary bone develops everywhere from the mesenchyme through the medium of osteoblasts, and not indirectly, as already described above, from calcification and ossification of connective tissue. Lubosch⁶ was in full agreement with the opinion of Schaffer⁷ that all bone arises

⁶ Lubosch Die Osteoblasten und ihre Metamorphose, Ztschr. f. mikr. Anat. 12:279, 1928

⁷ Schaffer: Die Verknöcherung des Unterkiefers und die Metaplasiefrage, usw., Arch. mikr. Anat. 32:266, 1888

through the participation of osteoblasts which are specific differentiated bone-forming cells of the embryonal mesenchyme. I am in accord with this view so far as it pertains to skeletal bone, and believe that all the embryonal primary bone is of osteoblastic origin. But how the osteoblasts form bone, that is, what the relation between the osteoblasts, fibrils, cement substance and the deposition of calcium is, are involved questions, the answers to which are not necessary for an understanding of the structure of fiber bone.

FINE-FIBERED OR LAMELLAR BONE

Lamellar bone replaces the original coarse-fibered bone, and by about the fourth year nearly the entire human skeleton consists of lamellar bone. Heuler,⁸ in studying cross-sections of the shaft of the human femur and humerus, found that by the eleventh year the adult structure is reached and maintained with no change from then on. It has been mentioned that coarse-fibered bone is the more important in the skeleton of a vertebrate, the lower it stands in the animal scale and the smaller its body. Gebhardt expressed the belief that the degree of formation of lamellar bone is related directly to the size of the skeleton, but of this there is some doubt.

Previous to birth the vascular spaces in the bone cortex are relatively large, and a coarse reticular structure is present. The size and shape of the vascular spaces at this time vary with the part of the shaft examined. The spaces are larger the nearer they are to the epiphyseal cartilage plate, and in the middle of the shaft of the diaphysis the spaces nearer the periosteum are larger. The primary haversian canals of coarse-fibered bone are the first spaces formed when bone is produced by the periosteum. In the course of development, many of these primary canals under the periosteum become confluent because of resorption of their walls and become the longer and more irregular haversian spaces. Shortly before and after birth osteoblasts deposit lamellae of fine-fibered bone on the coarse-fibered walls of these spaces, forming haversian systems. A haversian system consists of a central canal with bone deposited concentrically about it. At the same time, new trabeculae of coarse-fibered bone are formed subperiosteally. *A* and *B* of figure 4 are cross-sections through the middle of the shaft of an infant, aged 12 weeks, showing subperiosteal fiber bone with wide subperiosteal haversian spaces. Deeper in the cortex the canals have become reduced in size and some are surrounded by lamellar bone, though between the canals considerable coarse-fibered bone is still present. These first and

8. Heuler: Korrelation zwischen Alter und Knochenstruktur, *Ztschr. f. Zellf. u. mikr. Anat.* 7:41, 1928.

true haversian lamellar systems are also of temporary nature, and are resorbed and serve for the formation of new haversian systems. The process of formation and dissolution continues until the adult stage is reached, and even then a constant but slow reconstruction is continually taking place.

Beneath the periosteum, lamellar bone is laid down, and the surface of the bone finally consists of a series of lamellae. But various authors

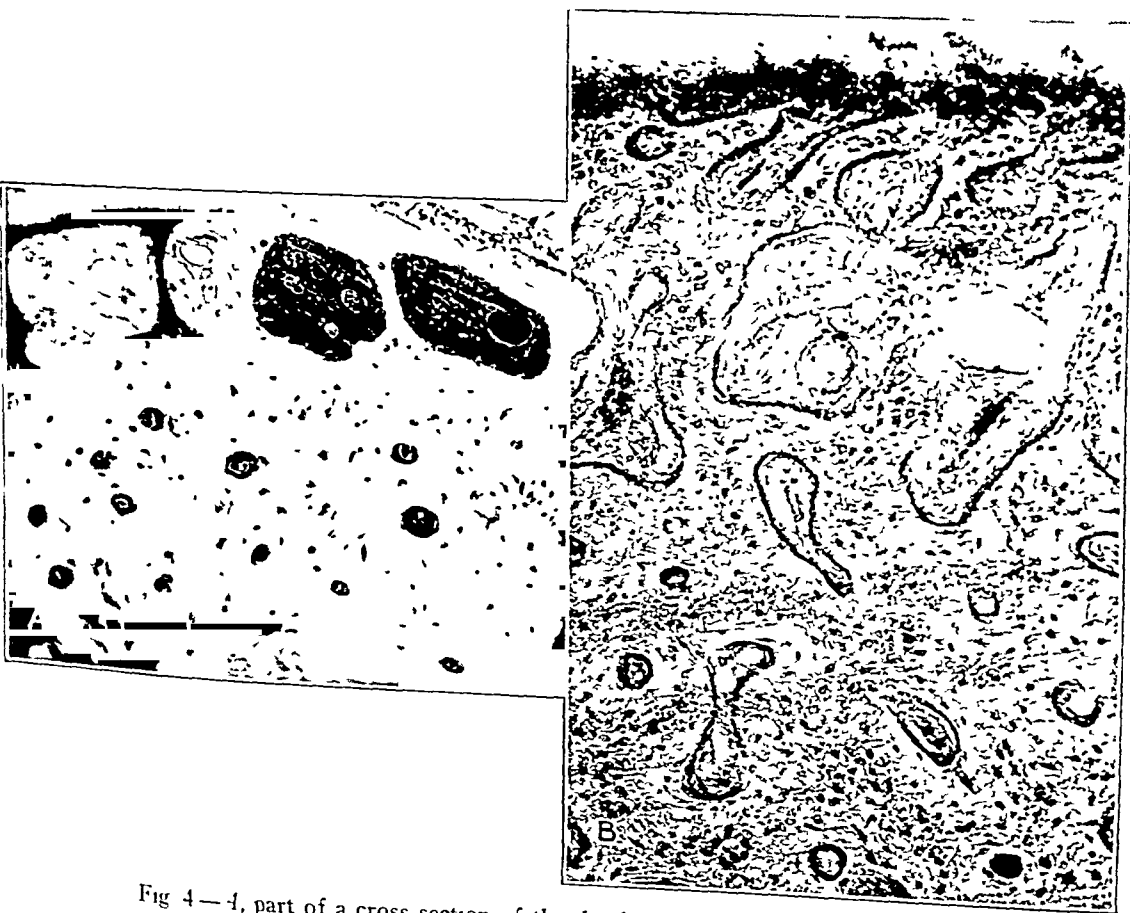


Fig 4—4, part of a cross-section of the diaphysis of a long bone of an infant, aged 12 weeks, showing wide subperiosteal haversian spaces underneath a thin layer of subperiosteal bone. Deeper in the cortex, the smaller haversian canals are seen. Carmine and Weigert's fibrin stain. B, part of cross-section through another long bone of the same infant. It is an unstained frozen section of von Ebner decalcified bone, showing the periosteum above with the subjacent large haversian spaces, and the deeper haversian canals, some of which are surrounded by a few concentric lamellae.

have described the first appearance of subperiosteal lamellar bone at different times. In long bones Schwalbe⁹ found fiber bone beneath the

⁹ Schwalbe Ueber postembryonales Knochenwachstum, Sitzungsber d med naturw Gesellsch zu Jena, 1877, p 11

periosteum until the fourth year. Koelliker reported subperiosteal lamellar bone as early as the first year after birth. Recently, authors have described subperiosteal lamellar bone in the first months after birth. I saw no subperiosteal lamellae in cross-sections through the shafts of two long bones of an infant, aged 12 weeks, though lamellar bone was present deeper in the cortex. On the larger endochondrally formed trabeculae in the marrow cavity, some lamellar bone is seen after birth.

General Structure of Lamellar Bone.—When an adult tubular bone is sawed open longitudinally, parts of it are seen to be dense and compact in texture and other parts, spongy. Accordingly, two forms of adult osseous tissue are distinguishable, compact and spongy bone. On closer examination, however, especially with the aid of a magnifying glass, it will be found that bone is everywhere more or less porous, and that the difference between compact and spongy bone depends in part on the different amounts of calcified tissue compared with the size and number of open spaces in each. The cavities are small in the compact parts of the bone, with much dense bone between them, while in the spongy texture the spaces are large, and the intervening bony partitions are thin and slender. When both compact and spongy bone are present, as, for instance, in the upper end of a tubular bone, there is no abrupt limit between the two; they pass into one another by degrees; the haversian spaces of the compact bone widen out, and the reticulations of the cancellated bone become closer as they approach each other.

In all bones, the outside is compact and forms a shell or crust of varying thickness, while the spongy bone is contained within. In a long bone the large round ends are made up of spongy tissue with only a thin coating of compacta; in the hollow shaft, on the other hand, spongy bone is scanty or absent, and the walls are formed of compact bone, which increases in thickness toward the middle, at which point the girth of the bone is usually least. In flat bones, such as those of the skull, the compact tissue forms two plates or tables, enclosing between them the spongy texture, which in such bones is named diploe. The short round bones, as the bones of the wrist, are spongy throughout, except at their surface, where there is a thin crust of compact substance. In the irregular or mixed bone, as, for example, a vertebra, the two types of bone have the same general relation to each other, but the relative amount of each in different parts, varies.

THE COMPACTA

A cross-section of the cortex of a bone shows that there are several ways in which the lamellae are arranged in the compacta. Some are deposited about blood vessels, as the haversian lamellae, to form the

haversian systems, and others do not surround blood vessels but are deposited by periosteum or endosteum, and are known as the outer and inner concentric or ground lamellae. In addition there are the interstitial lamellae which fill in the spaces between the haversian systems (figs. 5, 6 and 7).

In making comparative studies, it becomes evident that the structure of the compacta varies considerably. For instance, the structure was found to be quite different in various segments of the same circumfer-



Fig. 5.—A ground disk of the compacta of the diaphysis of a long bone, showing the outer ground lamellae, haversian systems and interstitial lamellae.

ence of the diaphysis. It was also found that sections through the shaft of various bones of the same person show varying degrees of development of the ground, interstitial and haversian lamellae. Examination of sections of corresponding bones of the rat, guinea-pig and rabbit shows marked variation in the degree of development of the different types of lamellar bone. For instance, a section of the tibia of the rat shows marked development of the outer ground lamellae, the haversian lamellae being few and the inner ground lamellae also being poorly developed. A section through the same bone of a guinea-pig shows better development of the inner ground lamellae, fewer outer

ground lamellae and better developed haversian lamellae. A section through the tibia of a rabbit shows still better development of the haversian lamellae at the expense of the ground lamellae. The dog shows haversian systems still more highly developed, but generally not as irregular as the haversian systems of the human cortex.

The Canals.—A system of preformed canals in the cortex carries blood through the compacta. These canals are known as the haversian canals, Schwalbe's canals, and the communicating canals, some of which are true Volkmann's canals. The haversian canals are found in the compacta, surrounded by concentric lamellae and running longitudinally through the bone. The canals of Schwalbe are found running circum-



Fig. 6.—Another portion of the ground disk, in figure 5, showing the inner ground lamellae below, haversian systems and interstitial lamellae.

ferentially between the ground lamellae or transversely through them. The communicating canals connect the haversian canals; they run transversely or diagonally through the shaft and sometimes, when they are not preformed, are true Volkmann canals.

Haversian Systems.—The haversian system constitutes the basic structural unit of lamellar bone, and a knowledge of its structure and formation is necessary for a clear understanding of the anatomy of adult bone. The formation of this type of bone is ascribed to osteoblasts by all workers who believe that the osteoblasts are bone formers. The osteoblasts deposit the haversian lamellae in layers on the coarse-fibered bone about the walls of the blood vessels in the primary marrow

spaces, thus forming the first haversian systems. The osteoblasts are carried into the fiber bone by the vessels. I agree with those who believe in the specificity of the osteoblasts in the formation of lamellar bone. But how the various constituents of the lamellae are formed opens up questions that I do not want to discuss here, for it involves complex and unsettled problems of bone formation. It seems to me that for the present, it is best to visualize the process of the replacement of coarse-fibered bone by lamellar bone as follows: The osteoblasts about the vessel deposit a layer of osseous material on the fiber bone. As a result, a cylinder is formed which is known as a haversian lamella. As the lamellar bone is deposited on the fiber bone, the latter gives way. The replacement does not occur through the medium of erosion or osteoclasts, but as a process of substitution, in which the fiber bone tacitly disappears. Certain of the chemical components of the fiber bone

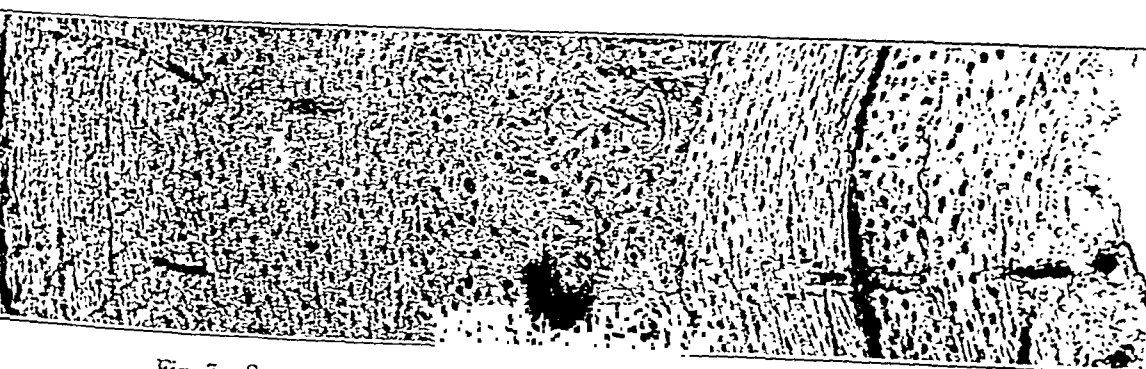


Fig. 7.—Segment of a cross-section through the diaphysis of the tibia of a guinea-pig, showing the well developed outer ground lamellae, a narrow zone of haversian systems, and well developed inner ground lamellae. Unstained frozen section of von Ebner decalcified bone.

are utilized by the lamellar bone in the reconstruction. Marchand,¹⁰ in describing the creeping replacement of transplants to which this process is akin, said that when the first lamella is formed, one cell process from each cell of the ring of osteoblasts about the vessel enters it. A few cells leave the original row of osteoblasts, become enclosed in the bone ground substance and become bone cells. The original osteoblastic row is again closed by multiplication of its cells; the process is repeated; a new cylinder is formed between the first cylinder and the blood vessel, just external to the osteoblastic layer. Cells from the osteoblastic layer invade this new bone ground substance, and a second lamella is completed. In this way the haversian columns become stratified structures forming haversian systems made up of haversian lamellae, traversed by a central canal containing vessels.

10. Marchand: Prozess der Wundheilung. Deutsche Chir., 1901, vol. 16.

How the first lamella expands to accommodate the succeeding ones is not made clear in the literature. It is evident that the lamellae are being formed rapidly and that they are not rigid when formed, so that expansion by pressure of the newer lamellae is possible. Also, in the formation of the haversian systems, as the lamellae are laid down, the vessel space is encroached on and the original space is reduced in size, for the haversian canals of normal lamellar bone are generally much smaller than the vascular spaces of fiber bone. Thus the lamellar bone formed about the vessel probably grows centrifugally and centripetally.

The lamellae about the haversian canals are disposed in a ringlike manner, but sometimes they do not extend entirely around the canal. This occurs where one canal is anastomosing with another. In the region of the anastomosis, the lamellae frequently surround the anastomotic vessel. The size and shape of the haversian systems of human bone vary considerably on account of the reconstruction that is constantly taking place. In general it may be said that the widest haversian canals are surrounded by the fewest lamellae, the medium-sized canals by the largest number of lamellae, while the smallest canals also possess thin walls, though they are thicker than the walls of the widest canals.

According to Koelliker, the thickness of the individual lamellae of human bone varies from 4.5 to 11 microns, the average thickness being from 6.7 to 9 microns. Von Ebner gave from 3 to 5 microns as the average thickness of the lamellae, but most were 3 microns thick. My own figures approach more nearly to those of Koelliker. The number of lamellae in each haversian system is, as a rule, from 8 to 15; sometimes only 4 or 5 are present; sometimes from 18 to 22 are seen. The haversian systems constitute most of the thickness of the diaphysis in man and are separated from the periosteum by the outer ground lamellae. Sometimes, the haversian systems even penetrate the outer ground lamellae, while the latter may sometimes enter between the more superficial haversian systems. When inner ground lamellae are present, they separate the haversian systems from the marrow cavity.

Bone Cells.—The lamellae are traversed by the canaliculi and processes of the bone cells while the lacunae, containing the bone cells, are either in the lamellae near the borders or between two lamellae. Most of them are between the lamellae. The lacunae of adult bone are minute elliptic recesses in the bone and extending from them are fine pores or tubes called canaliculi which issue from their cavities. These canaliculi are numerous, slender and relatively straight. They come off from the surfaces of the lacunae, as they may be seen in both longitudinal and cross-sections. They are more numerous in cross-sections. The lacunae present some differences in shape, but in a cross-section they appear irregularly fusiform, for the most part, and lie

nearly in the same direction as the lamellae between which they are situated. That is, the little cavities are flattened and extend conformably with the lamellae. When the bone is cut longitudinally, sections of the lacunae will still appear fusiform and lengthened out in the direction of the lamellae. The canaliculi, on the other hand, pass across the lamellae and communicate with those of the neighboring lacunae so as to connect the lacunae with one another (fig. 8 *A* and *B*). Since the canaliculi of the most centrally placed lacunae open into the haversian canals, a system of continuous passages is established by these tubules and their lacunae, along which fluid may be conducted from the haversian canal

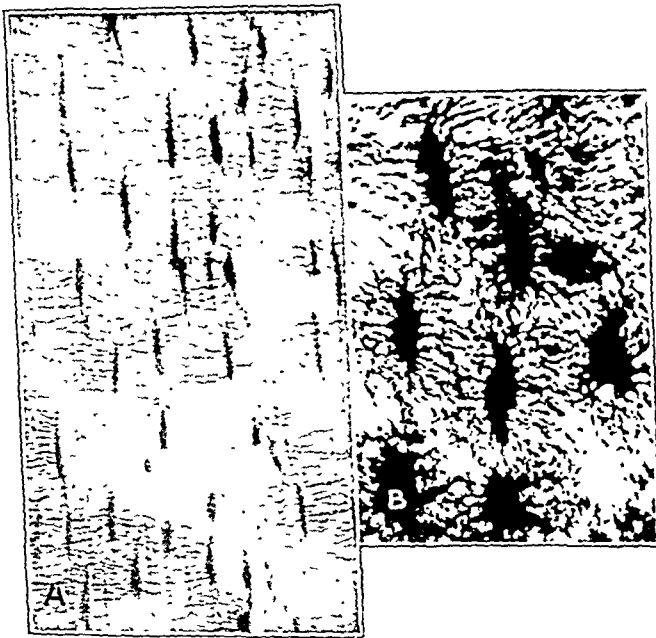


Fig. 8.—*A*, bone lacunae and canaliculi of human bone, showing anastomoses of canaliculi. A longitudinal ground disk mounted in balsam. *B*, lacunae and canaliculi of human bone in a ground disk impregnated with silver according to the method of Matschinsky.

through its surrounding lamellae. It seems probable that the chief purpose of these minute passages is to convey nutrient fluid from the vascular haversian canals through the mass of hard bone that lies around and between them. In a like manner, the canaliculi open into the main marrow cavity and into the marrow spaces between the spongy trabeculae, for the spongy bone also contains lacunae. Each lacuna is occupied by a nucleated bone cell, the walls of which are applied to the inside of the cavity, while branches or tubular protoplasmic processes line the canaliculi and anastomose with intracanalicular branches of similar cells, which occupy neighboring lacunae.

On the surface of the haversian canals osteoblasts are seen, varying in number in the different canals. In adult lamellar bone, just a few are seen.

The Fibrillar Structure of the Haversian Lamellae.—Each lamella consists of innumerable fibrillae embedded in a cement substance, with calcium salts impregnated between the fibrils. Together these elements constitute the ground substance of the bone. If a cross-section of the cortex, in the form of a ground disk or a frozen section, is examined under the polarizing microscope, oil immersion being used, the lamellae present a stippled appearance, each point being 1 micron or less in diameter. The points are closely applied and represent cross-sections of individual bone fibrils. Unless the section is in focus, the stippled appearance is not seen. It may be brought out by pressing the slide vigorously against the stage of the microscope. A longitudinal section of the bone examined in the same way shows a serially striated appearance. In such a section, the striations also represent individual fibrils. Heating the section will bring out the fibrillar structure a little better. The decalcification of bone, hydrochloric acid being used, in no way injures the fibrils.

That the fibrils of bone possess the qualities of fibrils of connective tissue may be seen by the treatment of sections with acetic acid, which causes the fibrils to swell and disappear. If they are countertreated with alkalis the fibrils will reappear, but with overtreatment with alkalis the fibrils will again disappear. Another fact in favor of the similarity of connective tissue and bone fibrils is that collagen can be extracted from both bone and connective tissue.

It is generally believed that the inorganic salts of the ground substance do not become chemically combined with the collagenous fibrils. While a cement substance is believed to be present between fibrils, the unequivocal demonstration of the nature of this material is difficult. Its existence is inferred from the fact that in disks and sections the fibrils are separated and seem to be embedded in a supporting material. Further evidence of the existence of cement substance is the observation of von Ebner that incineration of bone leads to the destruction of the fibrils, but the supporting material remains, and in it air-filled spaces formerly occupied by the fibrils may be demonstrated. The cement substance is supposed to consist of an organic base containing calcium salts. It is apparently the homolog of the cement substance of connective tissue. Since von Ebner made the classic studies of the fibrillar structure of lamellar bone, practically nothing new has been added. However, Henle, and Sharpey before him, had recognized the fibrillar nature of bone.

The uniformity of the arrangement and direction of fibrillar bundles and the delicacy of the fibrils are characteristic of lamellar bone. This

contrasts strikingly with fiber bone, in which the bundles are coarse, running parallel or interlacing. It is typical of lamellar bone that its fibril bundles are arranged concentrically. In haversian systems, this concentric arrangement is related to the haversian canal. In ground lamellae the concentric arrangement is related to the main marrow cavity, and in spongy bone the arrangement of the lamellae is related grossly to marrow cavities between the trabeculae (fig. 9 *A* and *B*).

The arrangement of the fibrillae in each lamella has been variously described. The question as to whether the fibrils and fibril bundles intertwine has been the main point on which there has been a difference

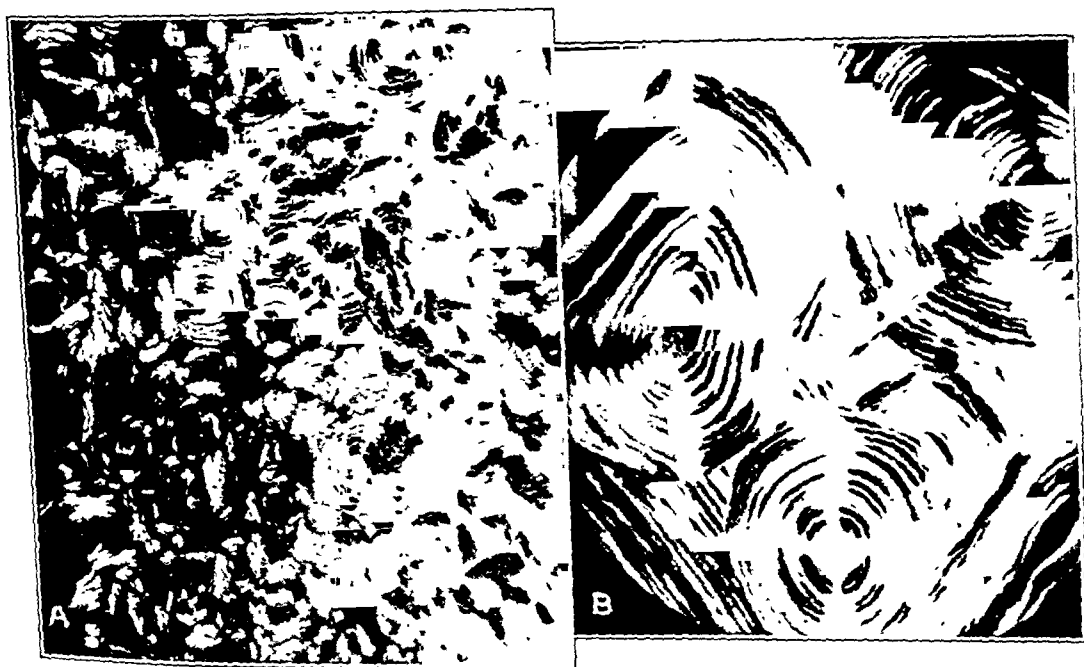


Fig. 9.—*A*, ground disk of cross-section of human bone as seen under the polarizing microscope. *B*, higher magnification of *A*, showing details of fibrillar structure of three haversian systems and some interstitial lamellae.

in opinion. Koelliker believed that fibrils were straight, and were arranged in closely adjacent straight bundles which did not connect. According to him, these bundles are perforated by numerous canaliculi, but their fibrils do not intertwine. Opposed to this view are the observations of von Ebner and Weidenreich.¹¹ Von Ebner described the fibrils as straight but intertwining, while Weidenreich said that the individual fibrils are twisted spirally and, in addition, intertwine.

11. Weidenreich: *Knochenstudien I. Teil: Ueber den Aufbau und Entwicklung des Knochens und den Charakter des Knochengewebes*, *Ztschr. f. d. ges. Anat.*, part 1; *Ztschr. f. Anat. u. Entwicklungsgesch.* 69:382, 1923.

According to the latter, each fibril bundle in lamellar bone contains only a few fibrils.

The fibril bundles of most lamellae, according to von Ebner and Gebhardt,¹² run spirally, making turns around the haversian canal at angles of approximately 45 degrees, but the degree of the angle may vary from 1 to 90 degrees in the different lamellae of each system, and some of the lamellae may have their fibers parallel to the canal. The general direction of the fibrils changes in each lamella of the haversian system, so that in one lamella the fibril bundles may run clockwise and in the next, counterclockwise, but in some haversian systems a few of the adjacent lamellae may show fibrils running in the same direction

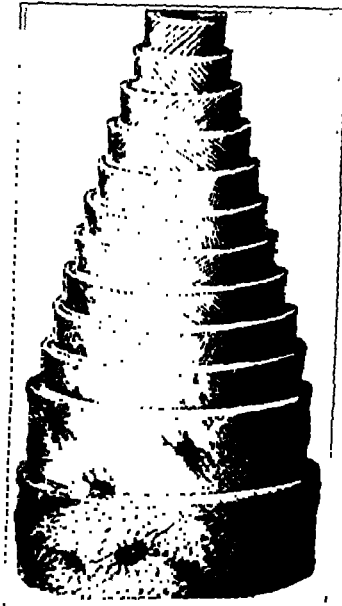


Fig. 10.—Diagrammatic representation of a haversian system, showing the haversian canal, the layers of lamellae with the fibrils running in alternating directions, and the bone cells with their anastomosing canaliculi. After Braus.

(fig. 10). It is believed by most observers that some of the fibrils of each lamella enter the adjacent lamella and in this way bind the lamellae together.

It must be remembered that the haversian lamellae, though disposed about central canals which run longitudinally, are frequently not completely concentrically arranged about the canal, because the diameter and the direction of the lumen of the canal may vary. Some lamellae do not completely encircle the canal because the haversian systems are being altered by reconstructional changes going on in them, which leads

12. Gebhardt: Ueber funktionell wichtige Anordnungsweisen der groeberen und feineren Bauelemente des Wirbeltierknochens, I & II, Arch. f. Entwicklungsmechn. d. Organ. 11:383, 1901; 20:187, 1905.

to irregular resorption within the canal and replacement of the old haversian system by newly deposited lamellae. As a result of resorption, the reconstruction does not produce the identical pattern of the bone but the result is a disordered reconstruction, with numerous irregular haversian systems and parts of systems of all sizes known as breccie. In adult human bone, there are few undisturbed haversian systems, especially as compared with animals. In the bones of the lower jaw and those of the hand and skull, the regularly formed haversian systems are even fewer in number than in the other bones.

The Ground Lamellae.—The compacta or cortex of the tubular bone of man consists, for the greatest part, of haversian systems. On the outer and inner surfaces of the compacta, there is often but not always a system of lamellae running parallel to these surfaces but not related to central blood vessels. These are the ground lamellae. The outer ground lamellae are under the periosteum, by which they are deposited on the haversian columns of the compacta. Since these are formed during the active growth of the bone, it sometimes happens that haversian systems formed later are enclosed in ground lamellae. Inner ground lamellae are present only in the diaphysis of long bones and run in the same general direction as do the outer ground lamellae. They are present in the diaphysis only when there is no spongy bone, that is, when the marrow is in contact with the compacta. These lamellae are deposited from the endosteum. The thickness of the outer and inner ground lamellae varies considerably in different tubular bones and may measure anywhere from 45 to 900 microns. Where the superficial or outer ground lamellae are best developed, some may be present between the haversian systems and may be called interstitial ground lamellae. If such ground lamellae are present, they must not be confused with the interstitial lamellae resulting from the breaking up of haversian systems. The interstitial ground lamellae may be differentiated from the interstitial lamellae that result from the breaking up of haversian systems by the fact that the former contain a few Sharpey fibers, while the latter do not.

The thickness of an individual ground lamella is about like that of an haversian lamella, and the number of ground lamellae varies between 10 and 100. The fine fibrils of the ground lamellae run like those in the haversian lamellae, but the direction of the fibrils may change within the same lamella. The ground lamellae are perforated transversely by Sharpey fibers.

The Interstitial Lamellae.—The interstitial lamellae must not be confused with the haversian lamellae when old haversian systems break. Their formation may be followed by studying cross-sections of compact bone. Existing haversian systems are being constantly resorbed on

the inner or vessel side and replaced by new haversian columns. The junction or line of demarcation of the resorption is represented in section by a shiny and irregular line. If the rate of new bone formation exceeds that of resorption, the old haversian system, that is, the system that is being replaced, splits up, and the fragments of the splintered haversian system fill the spaces between the haversian systems, producing the interstitial lamellae which are also called breccie. The haversian interstitial lamellae form an important supporting mass for the haversian columns of the compacta and nearly always run diagonally. These lamellae are of the same thickness as the haversian lamellae, and the fibrils retain the same appearance and course as existed in the haversian systems from which they formed. In the cortex of adult bone, in addition to the interstitial lamellae, small nests of typical coarse-fibered bone with some bone cells have occasionally been described.

The Cement Lines.—The haversian systems and fragments of haversian systems are separated from each other and from the ground lamellae by sharply defined lines. These were designated as cement lines by von Ebner, the term by which they are now known. These lines are generally quite irregular, though some may be straight. In general, they represent the site of resorption of lamellar bone, and on their surface, facing the haversian canal, new lamellar bone has been deposited. On an average, a cement line is thinner than a lamella, but it may be about as thick as a lamella. The cement lines are non-fibrillar (figs. 11 and 12). Von Ebner found that in the immediate vicinity of the cement lines new formed bone showed no lamellar structure but was made up of fibrils and irregularly distributed cells. This is best seen in the buckled regions of the cement lines, for where the cement lines are straight the lamellae are preserved. Von Ebner noticed that some bone cells lie on the border of the cement lines, which seem to cut them and their processes. He noticed also that the canaliculi of the bone cells in the region of the cement lines do not traverse them but turn away. This was confirmed by Matschinsky.¹³ Schaffer expressed the belief that while most of the canaliculi and bone cells in the region of the cement lines do not traverse them, some actually do and these communicate with the cells of the adjacent haversian systems. Weidenreich believed that anastomoses through the cement lines between the cells of different haversian systems exist, and are important in the transformation and growth of the formed bone. While preparations that my associates and I have made confirm the observations of von

13. Matschinsky: Ueber das normale Wachstum der Roehrenknochen des Menschen Arch. f. mikr. Anat. **39**:151, 1892.

Ebner, we found a few canaliculi which traversed the cement lines, as described by Schaffer.

The cement lines divide the bone into innumerable irregular islands of tissue. The union of these pieces at the cement lines is not as firm as the union of two individual lamellae through the medium of the fibrils and is dependent mainly on the interlocking of the adjacent pieces. In a specimen of macerated bone that had been exposed to the elements for a long time, we found that the lamellae held together very



Fig. 11.—Section through diaphysis of human bone from a case of osteomyelitis. The white lines are the cement lines and illustrate how the cortex is composed of innumerable irregular pieces cemented together. Frozen section stained by Bielschowsky's silver method.

well, but that the haversian systems separated from each other at the cement lines.

In illustration 226 of his "Handbuch der Gewebelehre." Koelliker demonstrated lines found regularly between the periosteal ground lamellae, though they varied in number and thickness. These lines contain no fibrillae of their own; in this respect, they are similar to the cement lines, but differ from them in that Sharpey fibers penetrate them. These lines contain bone cells and canaliculi or may be penetrated by

these structures. They are formed by a deposition of calcareous material in an interfibrillar cement substance and are therefore analogous to cement lines in structure. These lines are formed because bone is deposited underneath the periosteum rhythmically, and between two such lines one can determine the amount of growth that has occurred during a certain period. In the inner ground lamellae of a metacarpal bone, many such lines were found.

Sharpey Fibers.—Sharpey fibers were described under coarse-fibered or primary bone, and they were shown to constitute an important part of this bone. They were described as being present in periosteally formed bone, and being derived from the periosteum. In fine-fibered or lamellar bone, they are few. Sharpey described them as

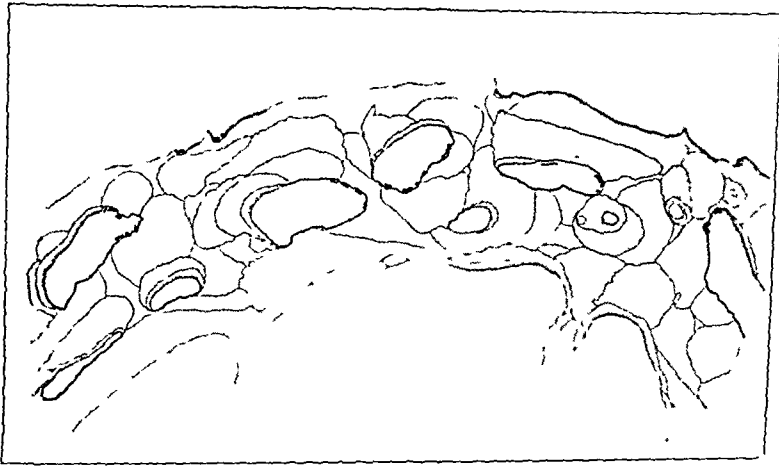


Fig. 12.—Diagrammatic representation of a cross-section of the shaft of a phalanx of a child, aged 6 years, showing the reconstructional changes going on, and the division of the cortex into innumerable pieces cemented together. After Burkhardt and Petersen.

fibers or fiber bundles which perforate the lamellae, passing through them in a perpendicular or more or less oblique direction. These perforating fibers may be seen with the aid of the microscope in a thin transverse slice of a decalcified cylindric or cranial bone when the ground lamellae are pulled apart. In this way some lamellae will be observed with fibrous processes attached to them which vary in length and usually taper and are pointed at the free extremities but sometimes are abruptly truncated. These fibers have obviously been drawn out from the adjacent lamellae through several of which they must have penetrated. Sometimes, indeed, indications of perforation may be recognized in the part of the section of bone from which the fibers have been pulled out. The processes in question are viewed in profile but they may frequently be seen on the flat surface of detached lamellae, pro-

jecting like nails driven perpendicularly or slantingly through a board, while other lamellae present obvious apertures of considerable size through which perforating fibers have passed. These fibers may also be demonstrated by staining methods. They may be demonstrated in animals like adult guinea-pigs, in which the ground lamellae are well developed, by teasing apart the outer ground lamellae in a thick frozen section.

While some experimenters have been unable to find Sharpey fibers in adult human bone, and this is probably due to the fact that in such bone, ground lamellae may be few or absent. Koelliker and Weidenreich claimed to have demonstrated them in small numbers in subjects up to 60 years of age. In adult bone, Weidenreich and Koelliker found them only in the outer ground lamellae which are derived from the periosteum, and they showed variation in quantity and thickness. According to von Ebner, they appear infrequently in the haversian systems of adult bone. Braus¹⁴ described and illustrated them as occurring in all lamellae, but this is denied by almost all other workers. Weidenreich believed that Sharpey fibers end abruptly at the cement lines. They are estimated as 3 mm. in length in adult human bone. They are believed to prevent the displacement of the ground lamellae. As they pass through the lamellae they sometimes branch, and these branches are directed toward the surface of the bone. They may be quite thick, and nests of these fibers may sometimes occupy a large area in the ground lamellae, and they may have a few bone cells embedded in them. They may then simulate an ossified tendon insertion.

Elastic Fibers.—Von Ebner and Koelliker believed that elastic fibers are found, though seldom, in outer ground lamellae, and according to them some Sharpey fibers are elastic fibers. Von Ebner also described elastic fibers in the innermost lamellae of the haversian system and believed that these fibers were found only in adults. Weidenreich found many elastic fibers in the outer zone of the periosteum, a few in coarse-fibered bone, but none in lamellar bone. On the other hand, Maier¹⁵ and Tafani¹⁶ believed all Sharpey fibers to be elastic fibers. However, the consensus of opinion is that there are few elastic fibers in bone. While some elastic fibers mingle with the Sharpey fibers, others are independent of these fibers, and may accompany the vessels of the cortex.

14. Braus: *Anatomie des Menschen*, I Bewegungsapparat, Berlin, Julius Springer, 1921, p. 835.

15. Maier: *Die elastischen Fasern des Knochens*, Virchows Arch. f. path. Anat. 26:358, 1863.

16. Tafani: *Le tissu des os, les fibres perforantes ou de Sharpey*, Arch. ital. di biol. 8:66, 1887.

THE SPONGIOSA

Origin.—Spongy bone makes up most of the mass of the smaller bones like those of the tarsus, carpus, the bodies of the vertebrae and ribs, and the upper and lower ends of tubular bones. While considerable literature exists under the title of spongy bone, most of this literature deals with the question of the influence of the mechanical factors of stress and strain on the architecture of spongy bone, rather than with the question of origin, reconstruction and relation of this bone to the compacta. Furthermore, there has crept into the literature the erroneous statement that all spongy bone is formed from the inner surface of the cortex by a peeling off process, in the course of which cortical haversian

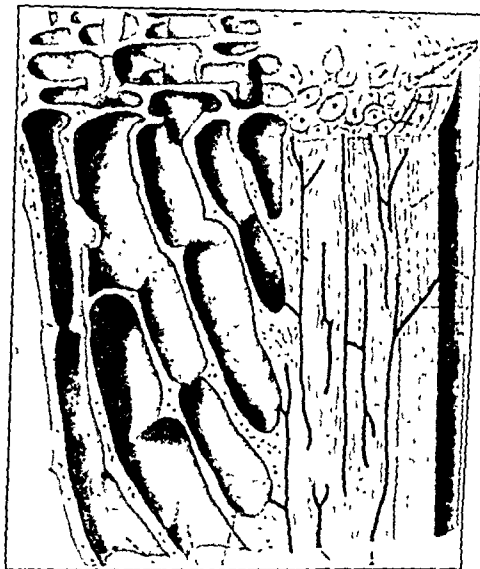


Fig. 13.—Diagrammatic representation of a longitudinal view of a bone, showing both compacta and spongiosa. The cortex on the right shows the outer ground lamellae, with some Sharpey fibers penetrating them. The haversian systems are illustrated, and the longitudinally directed haversian canals are shown. The spongy trabeculae and lamellae are illustrated in the left half of the picture. After Braus.

systems have been widened through resorption by osteoclasts from within the haversian canals. This conception has arisen as a result of the observation, particularly in the upper end of the femur, that some spongy trabeculae are attached at their base to the inside of the compacta. That some spongy trabeculae arise in this way, particularly in the diaphysis, there is no doubt, but in general this conception is wrong.

Structure.—On close inspection, adult spongy bone is found to be composed of slender bars or spicules or thin lamellae of bone which meet and join in a reticular manner, producing an open structure which has been compared to lattice work (figs. 13 and 14). In this way con-

siderable strength is attained without undue weight, and it may usually be observed that the strongest laminae run through the structure in those directions in which the bone naturally has to sustain the greatest pressure. The open spaces or alveoli of the bony network communicate freely. In the fresh state, they contain marrow and blood vessels and give support to these structures.

Due to the variety of the forms of the components of spongy bone, they have been designated by many names. Roux¹⁷ divided the components of spongy bone as follows; (1) tubes (tubuli), (2) hemispherical spaces (pilae), (3) plates (lamellae) and (4) beams (trabeculae). The tubuli ossei are the long spaces in spongy bone enclosed by the thicker trabeculae, and the pilae ossei are curved spaces in spongy



Fig. 14.—A large and more detailed diagrammatic representation of the spongy bone, shown in figure 13. The construction of the trabeculae is plainly seen at the upper surface of the drawing and the surfaces of the lamellae are also seen. The tubuli between the lamellae are represented. The apertures in the lamellae by which the tubuli connect are shown. After Braus.

bone, particularly underneath the articular cartilage and are enclosed by the thinner lamellae. Where the trabeculae or thin lamellae cross each other, a netlike spongy bone is produced. This division of the elements of spongy bone is a rough evaluation, because there are innumerable transition forms and shapes which make a strict terminology impossible. The lamellae and trabeculae of the spongy bone show numerous fine apertures. The marrow spaces which are separated by the trabeculae or lamellae communicate with each other through the apertures. In places the apertures show a regular arrangement, forming pairs of openings placed above each other. The flat surface of the lamella then

17. Roux: Die Entwicklungsmechanik, Vortr. u. Aufs. u. Entwicklungsmech. d. Organ., 1905, nos. 1 to 5.

appears as a strainer. Sometimes larger holes are present, and the face of the lamella appears latticelike.

When the end of the diaphysis of a long bone is examined, it is seen that the cortex becomes thinner from the point where spongy bone appears in considerable amounts. This thinning of the cortex does not necessarily occur uniformly throughout the same horizontal plane of the bone. As was pointed out, the belief is that the cortex thins out because it gives rise to the spongy lamellae, but it must again be emphasized that all the spongy lamellae certainly do not arise from the cortex and that in the epiphyseal ends of the bone the cortex is always thin or inconsequential and the spongy bone is considerable. The appearance

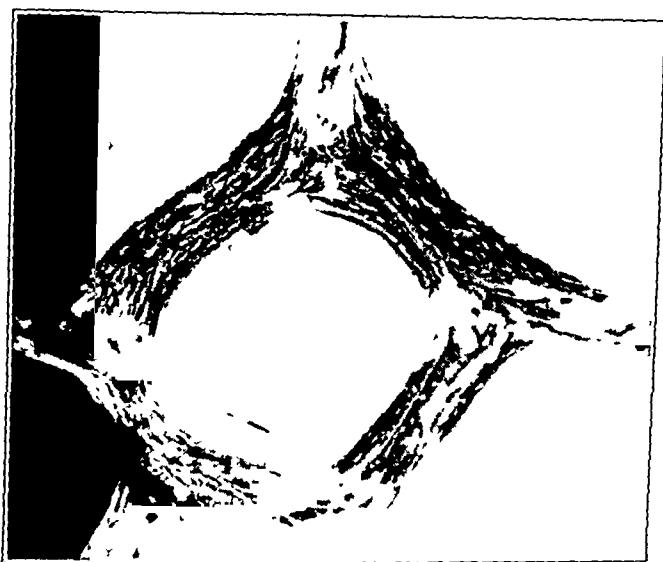


Fig. 15.—Details of structure of a lamella of spongy bone in a ground disk examined with polarized light.

of laminae of bone arising from the cortex is due rather to the spongy lamellae and trabeculae fusing with the cortex.

The spongy trabeculae and lamellae differ from the haversian systems in that only the larger trabeculae contain blood vessels, and compared with the cortex the vessels are few. When trabeculae contain blood vessels, they are surrounded by concentric lamellae. The inner part of a spongy trabecula is composed of small pieces, the breccie, on which layers of lamellar bone are deposited. These breccie consist of small, angular pieces of lamellar bone and are similar to the interstitial lamellae. The lamellae, of which the breccie are comprised, frequently run diagonally to the lamellae on the surface of the trabeculae, and in one trabecula several breccie may be seen, each directed at a different angle. The outer surface of the trabeculae is composed of lamellae which are laid down somewhat concentrically around the marrow spaces.

A few osteoblasts line the trabeculae of adult bone. The trabeculae contain bone cells which anastomose with each other. The fibrillar structure of the trabeculae is no different from that in the lamellar systems. However, the details of the fibrillar arrangement in spongy bone seem not to have been widely investigated. The active cellular bone marrow is supported in the meshes between the spongy bone; and in the diaphysis of long bones of adults, in which the spongy trabeculae are few or entirely absent, the marrow is fatty (fig. 15).

THE RELATION OF FUNCTION TO THE STRUCTURE OF BONE;
WOLFF'S LAW

When the spongy lamellae and trabeculae in the neck of the femur are examined, they are seen to course in archiform effect from one inner wall of the bone to the opposite wall. They cross each other at nearly right angles, and their points of intersection lie nearer that cortex from which the lamellae seem to be separating at the more acute angle. The spongy lamellae and trabeculae as they seem to come off from the cortex make more acute angles the further up they are in the shaft. However, in other bones, like the vertebrae, while the spongy lamellae and trabeculae cross each other to form spaces, there is no particular arrangement of the spongy bone such as occurs in the upper end of the femur.

On the basis of the appearance of the spongy bone in the upper end of the femur, there has been developed the theory of the transformation of bone due to mechanical influences exerted on it. The inner architecture of the spongy bone in this region, that is, the direction and contour of its trabeculae, is supposed to be conditioned by external stresses and strains exerted on the bone. In spite of the large literature and the immense amount of work that has been done on this subject, there is still much difference of opinion as to the proper interpretation of the inner structure of the femur.

The Origin of the Conception of Wolff's Law.—Those who maintain the view that bone is transformed by mechanical influences exerted on it base their beliefs on the observations that the mechanical structure of the normal femur conforms closely to the mathematical proportions of a structure of similar shape and physical properties, the Fairbairn crane, which is designed to resist the action of loads similar in amount and manner of application to those sustained by the human femur. This led to the conclusion that the details of the inner structure of the femur are based on exact mathematical laws, and further, that the form of bone is adapted to its functions.

It is argued that if the external form and inner architecture of a normal bone represent the adaptation to normal function, then alterations in the mechanical demands made on normal bones should be

followed by corresponding changes in both the internal and the external structure. Such changes should produce a deformity, a marked change in contour, or a displacement from the natural normal position. Such changes of contour or displacement from the normal position are regarded as a physiologic adaptation of the structure to pathologic mechanical conditions, and therefore to pathologic function. The doctrine of the functional form of bone, with its corollary of the functional pathogenesis of deformity, has been ably set forth by Julius Wolff, but before him the problem of the mechanics of the inner structure of bone was much discussed. The history of the subject is well reviewed in the monographs of Wolff¹⁸ and Albert¹⁹ and in the more recent American paper by Koch.²⁰ The foundation on which this doctrine rests is the correspondence between the inner structure of the upper end of the femur and the lines of stress in the Fairbairn crane. The analysis of the crane was made by the mathematician, Culmann, who observed that the cancelli of many bones were arranged in forms similar to those which he had computed as the lines of maximum internal stress in a Fairbairn crane having a form which was assumed to approximate that of the upper fourth of the femur. The conclusion was that the cancelli lie along the paths of maximum internal stress and thus transmit a maximum load in the bone with a minimum of material. This observation of Culmann is the mathematical basis of the modern theory of the functional form of bone, and this theory has been criticized on purely mathematical grounds.

The Law.—In 1892, Wolff developed his theory of the relation of the internal structure of bone to function and dealt with the transformation of bone in normal and pathologic cases and discussed in considerable detail the structural changes in bone due to changed mechanical conditions. This work is abundantly illustrated with examples of many rare deformities, taken from collections in the principal museums of Germany. Culmann's mathematical analysis of the lines of stress in the Fairbairn crane and the somewhat analogous direction of the trabeculae in the upper femur are cited by Wolff as mathematical proofs that the architecture of the spongy bone of the neck of the femur follows exact mathematical laws, and that the form and inner structure of bone are determined by the mechanical conditions present.

Recently, Koch published an exhaustive study on the laws of bone architecture. His paper was directed toward bringing definite mathematical proof of the law. He arrived at the same conclusions as Wolff

18. Wolff: *Das Gesetz der Transformation der Knochen*, 1892.

19. Albert: *Einfuehrung in das Studium der Architektur der Roehrenknochen*, Wien., 1900.

20. Koch: *Laws of Bone Architecture*, *Am. J. Anat.* **21**:177, 1917.

did, that the normal external form and internal architecture of the human femur result from an adaptation of form to the normal mechanical demands on, or normal function of, this bone. He stated that the proportions of the femur are everywhere such as to show a definite mathematical relationship between the body weight and the internal structure of the bone; there is a definite relation between the structure and the stress at every point. According to him, spongy bone is homogeneous with compact bone as a structural material and differs from it mechanically only in possessing less strength, which is approximately in proportion to its density as compared with compact bone.

The general law of bone, the adaptation of form to function, holds true mathematically and mechanically in the normal human femur, and therefore, Koch concluded, for all other normal human bones. According to him a foundation is laid for the study and mechanical analysis of the spongy bone entering into the structure of other parts of the skeleton, by the application of the principle that spongy bone and compact bone are homogeneous materials and differ chiefly in strength, approximately in proportion to their densities. The thickness and closeness of spacing of trabeculae in bone vary directly with the intensity of the stresses transmitted by them.

This theory of the functional forms of bone with that of the functional pathogenesis of deformity has been accepted by many surgeons and orthopedists as a working basis in the treatment of deformities, but it has been the subject of so much controversy that much confusion has arisen as to the value of the theory in everyday practice.

Objections to the Law.—Wolff's doctrines of the functional form of bone and the functional pathogenesis of deformity have been vigorously assailed on various grounds by many investigators. Even those who have partly accepted the Wolff-Roux conceptions still feel that in addition to mechanical factors which influence the form and structure of bone, phylogenetic and developmental factors are at work. Even Gebhardt, who was a pupil of Roux, admitted that there are other than mechanical factors influencing the structure of bone. Von Recklinghausen,²¹ although in the main agreeing with the mechanical view, expressed himself as believing that the mechanical views are not sufficient to explain the internal architecture of bone entirely. Friedlaender²² laid most stress on the direction of the vessels in determining the internal architecture of bone. He also stated that much more significance must be attached to the factors of development. Triepel²³

21. Von Recklinghausen: Normale und pathologische Architekturen der Knochen, Deutsche med. Wchnschr. 19:506, 1893.

22. Friedlaender: Beitrag zur Kenntnis der Architektur spongiöser Knochen, Anat. Hefte 23:235, 1904.

23. Triepel: Die Architektur der Knochenspongiosa in neuer Auffassung, Ztschr. f. d. ges. Anat., part 2; Ztschr. f. Konstitutionslehre 8:269, 1922.

would also minimize the importance of the mechanical factors. Petersen²⁴ objected to the theory of Wolff and Roux on the grounds that the calculated direction of the main tension lines of the neck of the femur is not applicable to the bone, since these calculations, obtained from the Fairbairn crane, apply to homogeneous substances with the same elastic properties throughout. But bone is not homogeneous. It is made up of innumerable small pieces which are cemented together and which vary in size and number depending on the internal reconstruction which is always going on. According to Petersen, the determining factor in the structure of bone is functional activity which stimulates bone reconstruction through its effect on the cells, but function does not directly produce the internal structure by exerting a direct mechanical effect on the bone and thus causing the trabeculae and laminae to arrange themselves along certain lines of tension.

Most surgeons have more or less accepted the dicta of Wolff, but most anatomists and embryologists, while agreeing that mechanical factors may influence the inner structure of bone, are of the belief that the phylogenetic and hereditary factors are important, if not most important. It seems to me that this is the most logical point of view. Even if the trabeculae of the head of the femur were arranged in a way to conform with the mathematical principles as applied in the Fairbairn crane, nevertheless this fact could not be explained solely on mechanical grounds because the developmental influence could not be disregarded. In favor of this view is the fact that the trabeculae of all femurs are arranged in practically the same way, irrespective of mechanical influences exerted on them. Also every tissue constructs itself according to a certain pattern, and even in regeneration the original pattern is reconstructed. This is seen in the regeneration of a transplant, as of the thymus, which when placed in the abdominal wall reproduces thymic lobules with cortex and medulla. All tissues have an innate architectural pattern which they produce but which may be influenced by factors like nutrition, function and environment. And so I must agree with those who believe that the mechanical factors, though important, are only secondary in influencing the internal architecture of bone.

24. Petersen: Ueber Methoden zum Studium des Knochens, *Ztschr. f. wissensch. Mikr.* **43**:355, 1926.

SURGERY OF THE ESOPHAGUS*

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Surgical procedures have been employed for the relief of several pathologic conditions in the esophagus, the most common being the impaction of foreign bodies, cardiospasm, benign cicatricial stricture, carcinoma and diverticula. Impacted foreign bodies are now much less commonly dealt with by surgical means because of the easier and less dangerous method, in the hands of experts, of extraction through the esophagoscope, while surgical procedures have been almost eliminated from the treatment for cardiospasm. In this article the last three conditions, essentially, are considered.

Until within the past fifty years the esophagus received scant attention from the surgeon in spite of the well recognized pathologic conditions for which, theoretically, surgical procedures might well have been indicated. This is all the more striking when one remembers that the ancient Hindoos operated on the bladder for stone, and that Herophilus of the Alexandrian School used the knife boldly on such internal organs as the liver and spleen. For many years the only operative procedure attempted on the esophagus was esophagotomy of its cervical part. This was followed by the more complicated and drastic plastic operations and resections. The latter have so far been attended by a depressing mortality, so that some of the most stout-hearted surgeons often prefer to leave the anatomic relations of the viscus undisturbed rather than bring about almost certain death by surgical intervention. It is well known that when Billroth began to popularize his gastric operations he did so at the cost of many lives; yet nothing is more gratifying than the results of surgical methods in this sphere today. Moynihan¹ and Balfour² recently each reported a large series of

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1. Moynihan, Berkeley: *Two Lectures on Gastric and Duodenal Ulcer: A Record of Ten Years' Experience*, Bristol, John Wright & Sons, 1923, 48 pp.

2. Balfour, D. C.: *Fundamental Principles in Surgery of the Stomach and Duodenum: Report of 400 Cases*, *Surg. Gynec. Obst.* 42:167, 1926.

operations on the stomach with a mortality ranging from 1 to 2 per cent. Thus, by dint of perseverance and improvement in technic from time to time, that which was once a great risk has been converted into a safe every-day occurrence. This is not so in regard to esophageal surgery. The results of operative work in this sphere have been disappointing on the whole, in spite of modern advances in asepsis and technic. Esophagotomy can be performed fairly safely and diverticula can be removed without much risk, but carcinoma still claims its victims, operation in most cases serving only to hasten death. Still, some of those skilled in thoracic surgery, such as Torek, Meyer, Eggers and Lilienthal, have hopes that the time is not far distant when the surgeon will be able to wage war successfully against it. In his Hunterian Lecture, Abel³ took the same optimistic view.

Two facts stand out prominently in a consideration of surgery of the esophagus: (1) its comparatively recent history and (2) its slow and unsatisfactory progress. The undoubted cause of the first fact seems to be the relative inaccessibility of the esophagus, the viscus being deeply seated throughout its entire course. At first it took courage to make the deep dissection of the neck necessary for its exposure and surgical treatment. When this had been achieved it was probably thought impossible to expose the thoracic portion because of its intimate relations with such viscera as the pleura, lungs and aorta, injury to any of which must always be regarded with grave concern. For some time attempts were not made to lay bare the esophagus in its thoracic bed. Then came the development of the technic of posterior mediastinotomy whereby the esophagus could be reached without entrance to the pleural cavity. Later still, the invention of the differential-pressure chamber, by overcoming the well recognized occurrence of fatal postoperative pneumothorax, opened the road to the esophagus through the pleural cavity. Today it may be said that the surgeon's initial difficulty with regard to the esophagus, namely, that of overcoming its inaccessibility, has been solved. At least thus far has surgery of the esophagus progressed.

Although, as I have mentioned, the less severe operations of esophagotomy and extirpation of diverticula can usually be successfully performed, one seeks for explanations of why the more extensive operations, with a few exceptions, have been failures. Here one must remember that the final aim of the surgeon is to overcome carcinoma. Resection is therefore essential, and it is in the treatment of the esophagus after resection has been carried out that most of the difficulties which are at present preventing the progress of surgery in this sphere have arisen and still remain.

3. Abel, A. L.: The Treatment of Cancer of the Oesophagus, *Brit. J. Surg.* 14:131, 1926.

Theoretically, the operation of resection with end-to-end anastomosis is feasible; however, several factors exist to add to its risk and difficulty. At the present time, carcinoma of the esophagus is not diagnosed early enough. In most cases it would seem that this is due to the delay on the part of the patient in consulting a surgeon, but some patients with a very short history on examination are found to be suffering from extensive carcinoma. In either case, by the time the diagnosis is made the growth has invaded the esophageal wall to such an extent that the amount of the viscus to be removed in order to extirpate the carcinoma widely enough is much greater than that which would allow the cut ends to be brought together and sutured.

Assuming that a carcinoma is of such dimensions that when extirpated the cut ends of the esophagus can be brought together without undue tension, what other difficulties are there to overcome? The esophagus differs from the bowel in that it does not possess a serous covering. The significance of this is apparent. When the bowel is sutured, the peritoneum, in response to the traumatic irritation imposed on it, throws out lymph which coagulates, thereby sealing the line of suture. The surgeon does not get natural help of this sort from the esophagus, and consequently the safety of the suture of this viscus is greatly impaired. It is the general opinion that apart from the absence of help from serosa, the wall of the esophagus forms poor material for suture, both submucous and muscular coats being easily cut through. In this connection, Miller and Andrus found that if the lower third of a freshly removed human esophagus is divided and then joined by two layers of fine silk sutures grasping the submucosa, the artificial juncture withstands the pressure of a column of water 6 feet (182.9 cm.) high without the escape of either gas or fluid. From this investigation it is clear that the esophageal wall has the required strength, but the important point to be remembered is that in the living body its strength is dependent entirely on a sufficient blood supply.

Unfortunately, the esophagus is poorly supplied with blood although this is derived from several arteries, the aorta, inferior thyroids, subclavians, left inferior phrenic and left gastric. The great danger in end-to-end anastomosis of the esophagus is constriction of the blood vessels by the sutures, which is only too often the cause of necrosis with perforation of its wall and consequent leakage of its contents, resulting in fatal infection of the mediastinum or cellular planes of the neck. The loosening of the esophagus in its bed previous to resection, by necessitating severance of some of its blood vessels, will have already considerably diminished the nutrition of its cut ends, sometimes to such a degree that necrosis and gangrene ensue apart from any further diminution by constriction with sutures.

The outer coat of the esophagus consists of connective tissue continuous with that of the structures surrounding it. Carcinoma will usually be found to have invaded this and to have fixed the viscus. The loosening of the growth involves an opening of the cellular planes of the neck or the connective tissues of the mediastinum, and a grave risk is thereby incurred, because of the danger of ensuing cellulitis or mediastinitis which may take place in spite of the most careful aseptic precautions. This risk is always present, even when the esophagus is only loosened in its bed; however, if the lumen is opened, the risk increases considerably because of the highly infective nature of the esophageal secretion.

Coincident with the danger of mediastinitis is that of infection of the pleura, and the remarks concerning the former apply with equal force to the latter.

If the carcinoma extends through the esophageal wall the vagi are always involved and usually cannot be separated; they must be cut if resection is to be carried out. Although severance of these nerves does not always produce any apparent detrimental results, it is possible, and even probable, as Meyer pointed out, that interference with them plays a great part in bringing about the state of shock which has so many times proved fatal.

Lastly, the presence of the diaphragm has added considerably to the technical difficulties of operations on the lower end of the esophagus from the standpoint of resection of this part of the viscus and its substitution by stomach or intestine.

The chief reasons for the late inception of surgery of the esophagus, its relatively slow progress and its lack of attendant success can be summarized as follows:

1. The inaccessibility of the viscus; this applies particularly to the thoracic portion where its surgical approach is intimately bound up with previously developed operative procedures on the pleural cavity.

2. The absence of a serous coat in its cervical and thoracic parts.

3. A poor blood supply, interference with which often results in necrosis with tearing of sutures and extravasation of infective mucous secretion.

4. The danger of postoperative infection, cervical cellulitis, mediastinitis, pleurisy and empyema.

5. The probable danger of great shock resulting from interference with the vagi.

6. The presence of the diaphragm.

DEVELOPMENT OF ESOPHAGEAL SURGERY

The literature on surgery of the esophagus shows the great ingenuity that has been displayed by surgeons in their attempt to effect cures of the various pathologic conditions.

The earliest operations were essentially those of cervical esophagotomy, the simplest operation possible on the esophagus performed in its most accessible part for the extraction of foreign bodies. Thus, the first surgical measures were in the nature of emergency operations. Goursauld,⁴ in 1738, appears to have been the first surgeon to perform this operation. It was not found mentioned again until nearly a century afterward when Rolland,⁵ in 1819, performed it successfully. In 1833, Arnott,⁶ of the Middlesex Hospital, was the first Englishman to perform esophagotomy. The patient died fifty-six hours after the operation. Arnott remarked that he could not find any record of the operation having been done in England up to the time of his own attempt. In 1858, Cock⁷ said: "I can find but very few cases recorded in which the pharynx and esophagus have been opened for the purpose of extracting a foreign body." He himself successfully performed esophagotomy on a man who had swallowed a tooth plate.

In 1868, Cheever⁸ reported two successful cases and reviewed the literature on esophagotomy up to that time. He reviewed twenty-three other cases; however, the issue had not been successful in all. His list of surgeons contained the well known names of Syme and Nélaton, the latter being of the opinion that the operation was one of the gravest and most difficult in surgery.

The usual method employed for exposing the cervical esophagus and removing a foreign body was as follows: A left lateral incision was made along the inner border of the sternomastoid muscle from the level of the upper margin of the thyroid cartilage downward for about 10 cm., with incision through skin, platysma and deep fascia. If the anterior jugular vein was encountered, it was cut between ligatures. The omohyoid muscle was then either cut or retracted and the hyoid depressor muscles retracted medially while the sternomastoid was drawn laterally. The esophagus was found between the thyroid gland medially and the carotid sheath laterally and was incised longitudinally over the foreign body as far posteriorly as possible so as to lessen the risk of injury to the recurrent laryngeal nerve. The foreign body was then extracted and the esophageal wound closed with interrupted sutures or left open, the former practice being the more usual.

4. Goursauld, quoted by Cheever: *Two Cases of Esophagotomy for the Removal of Foreign Bodies*, ed. 2, Boston, J. Campbell, 1868.

5. Rolland, quoted by Cheever: *Two Cases of Esophagotomy for the Removal of Foreign Bodies*, ed. 2, Boston, J. Campbell, 1868.

6. Arnott, J. R.: *Case of Oesophagotomy*. *Tr. Med. Chir.*, London 18:86, 1833.

7. Cock, Edward: *A Case of Pharyngotomy for the Extraction of a Foreign Body*, with Some Remarks. *Guy's Hosp. Rep.* 4:217, 1858.

8. Cheever, D. W.: *Two cases of Esophagotomy for the Removal of Foreign Bodies*, with Some Remarks, ed. 2, Boston, J. Campbell, 1868.

There are a few points with regard to this operation which appeared in the literature at that time and which are worthy of note. There was a controversy as to the relative merits of a median and a lateral incision. The advocates of the former, among whom was Nélaton, preferred the median line with splitting of the thyroid cartilage so as to avoid injury to the recurrent laryngeal nerves. Those who recommended the lateral incision declared that with care these nerves could be avoided easily and that the exposure they obtained was superior to that obtained by their opponents. Whether or not a swelling appeared in the side of the neck after the impaction of a foreign body in the esophagus was given considerable attention. Several surgeons went so far as to say that the absence of swelling was a contraindication to operation. Again the advisability of ensuring drainage in case of leakage of secretion through the wound in the esophageal wall was well recognized.

At this time an attempt had not been made to expose the thoracic portion of the esophagus, and the only hope of extracting a foreign body impacted in that portion lay in being able to reach it from above through cervical esophagotomy or from below through gastrotomy. In 1886, because of this Richardson⁹ made some observations on the accessibility of foreign bodies fixed in this part of the esophagus. In experiments on cadavers he found that a finger introduced into the esophagus through a low incision in the neck could easily be brought into contact with a finger inserted upward through the stomach. As a result, he asserted that there was not a part of the esophagus which might not be reached with the finger either by gastrotomy below or by esophagotomy above. He also showed the easy distensibility of the cardia which allowed the introduction of two fingers up through it simultaneously, a distinct advantage to the operator attempting to free an impacted foreign body. These observations were of considerable practical value at that time. Since then the advent of the esophagoscope has dispensed almost entirely with the necessity of the extraction of impacted foreign bodies by the external route, because the danger entailed by the latter procedure is usually regarded as greater than that by the former.

As time went on it was only natural that surgeons should begin to devise ways and means of laying bare the thoracic part of the esophagus. It was natural, too, that an extrapleural route should be chosen because of the well recognized danger of pneumothorax resulting from opening of the pleural cavity.

⁹ Richardson, M. H.: A Case of Gastrotomy, Digital Exploration of the Esophagus and Removal of Plate of Teeth: Recovery, *Boston M. & S. J.* **115**:567, 1886; The Possibility of Operations on the Esophagus Through the Stomach as Shown by Dissections, *Lancet* **2**:707, 1887.

In 1888, Nasiloff¹⁰ working on the cadaver, resected from three to six ribs posteriorly, and through a vertical incision close to the vertebral column pushed forward the pleura, stripped it off the esophagus and thus exposed this structure extrapleurally. This is the first record in the literature of posterior mediastinotomy: the operation was a distinct advance not only in surgery of the esophagus but in thoracic surgery.

Quénu and Hartmann,¹¹ in 1891, and Potârcă,¹² in 1894, demonstrated subperiosteal resection of portions of the second to the sixth ribs on the cadaver, entering the posterior mediastinum and exposing the esophagus. They hoped that by this method of approach the resection of carcinoma of the esophagus would be feasible.

In 1895, Bryant¹³ devised another method of approach to the mediastinal portion of the esophagus. Instead of a straight vertical incision like that of Nasiloff,¹⁰ Quénu and Hartmann,¹¹ and Potârcă,¹² he made a quadrilateral flap with its base at the spinal column. The flap included all tissues down to the ribs and when it was raised from the underlying structures it was reflected medially. Three ribs were exposed and the middle one was resected for a length equal to that of the flap. The ribs above and below were divided only and turned medially with the intervening intercostal structures, forming a flap with its hinge near the vertebral column. After this the operation was carried on after the manner of Nasiloff and the esophagus exposed. Bryant demonstrated his method on the cadaver.

Rehn,¹⁴ in 1898, was apparently the first to employ a modification of Bryant's operation on the living subject. He made a large muscle flap with its base extending from the third to the ninth spinous process and then resected several ribs (an osteomuscular flap as devised by Bryant was not used). In the first operation he wounded the pleura; pneumothorax developed and the patient died six weeks after operation. In the second operation, the exposure of the carcinoma was satisfactorily carried out but the lesion was definitely inoperable. Suppuration of the wound and death on the sixth day followed. The esophagus was approached from the right side in both cases.

10. Nasiloff, J. J.: *Oesophagotomia et resectio eosophagi endothoracica*, St. Petersburg, Vrach, 1888, vol. 9, p. 481.

11. Quénu and Hartmann: *Des voies de pénétration chirurgicale dans le médiastin postérieur*, Bull. et mém. Soc. de chir. de Paris **17**:82, 1891.

12. Potârcă, I.: *L'oesophagotomie intrathoracique par le médiastin postérieur*, Roumanie Med. **2**:116, 1894.

13. Bryant, J. D.: *The Surgical Technique of Entry to the Posterior Mediastinum*, Tr. Am. Surg. A. **13**:443, 1895.

14. Rehn: *Operationen an dem Brustabschnitt der Speiseröhre*, Verhandl. d. deutsch. Gesellsch. f. Chir. **27**:448, 1898.

Llobet,¹⁵ in 1900, was the first to perform Nasilloff's operation on a human being, the case being one of benign stricture of the esophagus. Following a left paravertebral vertical incision and resection of several ribs, he pushed forward the pleura and exposed the esophagus without difficulty. There were two strictures which he incised longitudinally and then inserted a soft sound through the nose down into the stomach so as to model the lumen of the esophagus. The patient died eight days after operation. Purulent empyema was found at necropsy and was attributed to infection of the pleural cavity by the regurgitated gastric contents. Llobet called attention to the fact that he could have reached the esophagus in this position (just below the aortic arch) much better from the right side. He considered the operation feasible.

In 1901, Enderlen¹⁶ using the flap method, operated on a patient for the removal of a tooth plate in the thoracic portion of the esophagus. He extracted the plate successfully but in doing so injured the edges of the esophageal wound so severely that he decided not to suture but to drain. The patient was nourished through a previously made gastrostomy opening and although he was not well enough to be dismissed from observation until nine months after the operation, he recovered. Enderlen advised that the approach to the thoracic portion of the esophagus above the bifurcation of the trachea be made from the left side.

Henle,¹⁷ like Enderlen, performed posterior mediastinotomy for the removal of a foreign body in the esophagus. The patient died nine days after operation. In 1903, Faure¹⁸ and Tuffier¹⁹ exposed the esophagus by the posterior mediastinal route, but the patients died. Tuffier mentioned the transpleural route for exposure of the esophagus but believed that the danger from pneumothorax and pleural infection was almost too great.

By this time posterior mediastinotomy as an approach to the thoracic portion of the esophagus had become a recognized surgical procedure. There thus remain two approaches to be considered: the anterior mediastinal and the transpleural. The former is mentioned merely to be condemned. In Cairo in 1897, Milton²⁰ split the manubrium and body

15. Llobet, A. F.: *L'opération de Nassilov: La première intervention à Buenos Aires*, *Rev. de chir.* **21**:674, 1900.

16. Enderlen: *Ein Beitrag zur Chirurgie des hinteren Mediastinum*, *Deutsche Ztschr. f. Chir.* **61**:441, 1901.

17. Henle, quoted by Lilienthal: *Ann. Surg.* **74**:259, 1921; *ibid.* **76**:333, 1922.

18. Faure, J. L.: *Cancer de la portion thoracique de l'oesophage. Extirpation du néoplasme, par la voie médiastinale postérieure droite, combinée à une incision cervicale*, *Bull. et mém. Soc. de chir. de Paris* **29**:122, 1903.

19. Tuffier: *Sur la résection de l'oesophage thoracique*, *Presse méd.* **11**:364, 1903.

20. Milton, H.: *Mediastinal Surgery*, *Lancet* **1**:872, 1897.

of the sternum longitudinally in the median line and was able to pull the two halves about 6 cm. apart. This operation was undertaken for the removal of tuberculous lymph nodes, and it is easy to see that this procedure or any of its modifications as a means of reaching the esophagus extrapleurally is decidedly impracticable and well nigh impossible, because of the numerous important structures which lie in the way. Apart from this, the exposure of the esophagus, once it was obtained, would not be nearly so good as by the other two routes.

An Italian surgeon, Biondie,²¹ in 1895, was the first to attempt to explore the esophagus by the transpleural route; he used the dog as his subject. He employed a paravertebral incision followed by resection of two or three ribs. The pleura was incised, the pleural cavity opened, and the esophagus exposed by incision of the parietal pleura.

The opening of the pleural cavity for the intrathoracic operation on the esophagus or any other of the thoracic viscera was not put on a safe basis, however, until the invention of the differential-pressure chamber by Sauerbruch²² and the positive-pressure apparatus by Brauer and Petersen²³ in 1904. These inventions, by preventing collapse of the lung during operation and pneumothorax afterward, gave a great impetus to intrathoracic surgery, including that of the esophagus. They have been replaced largely by the simple method of intratracheal insufflation introduced by Meltzer and Auer²⁴ in 1909.

Now that the dangers of opening the pleural cavity have been overcome to such an extent that the surgeon need not hesitate to operate in it, there remains only the question of the type of incision to employ in order to get the required exposure. Dobromysslav, for example, used the flap method with subperiosteal resection of the underlying ribs. Sauerbruch introduced the simple intercostal incision of skin, muscles and pleura. This he found eminently suitable for experimental work on dogs, and it is still the most commonly used for that purpose. The usual procedure for opening the pleural cavity in man now includes either the division of ribs or their resection. Torek, in his famous case, cut down to the ribs through a curved incision, the anterior part of which was over the seventh intercostal space while the posterior part turned vertically upward near the vertebral column. He then divided the seventh, sixth and fifth ribs just lateral to their tubercles, and the

21. Biondie, D.: *Esophago-gastrostomia sperimentale intratoracica*, *Policlinico* (suppl.) 1895, p. 964.

22. Sauerbruch, Ferdinand: *Ueber die Ausschaltung der schädlichen Wirkung des Pneumothorax bei intrathorakalen Operationen*, *Zentralbl. f. Chir.* 31:146, 1904.

23. Brauer and Petersen: *Ueber eine wesentliche Vereinfachung der künstlichen Atmung nach Sauerbruch*, *Ztschr. f. physiol. Chem.* 41:299, 1904.

24. Meltzer, S. J., and Auer, John: *Continuous Respiration Without Respiratory Movements*, *J. Exper. Med.* 11:622, 1909.

pleural incision ran parallel to that in the skin. By retraction excellent exposure of the middle part of the pleural cavity was obtained and the esophagus easily reached. The level of the incision was planned according to the part to be explored.

The exposure of the posterior mediastinum for the laying bare of the thoracic portion of the esophagus extrapleurally has also received attention as time has gone on, and Lilienthal's²⁵ recent method, a modification of that employed by Torek, gives excellent exposure. His incision starts 20 or 22.5 cm. from the spine at whatever level he chooses and runs backward along a rib to the edge of the longitudinal spinal muscles and then curves upward parallel to the spine for four or five intercostal spaces. The rib over which the incision is made is resected subperiosteally, and the rib below and two or three above are divided just lateral to their tubercles. The usual care is taken in the ligation of intercostal vessels and the separation of the pleura from the periosteum of the ribs and intercostal muscles. By the introduction and spreading of a rib retractor, these ribs, which have been divided, are easily "shingled," one on top of the other, and thus exposure is obtained.

Grégoire's²⁶ extrapleural and extraperitoneal method of exposing the lower thoracic and cardiac segments of the esophagus is interesting and might well be mentioned. A U-shaped incision with unequal limbs is made on the left side of the thorax. It starts behind at the level of the eighth rib near the spine and runs vertically downward over the necks of the ribs until it reaches the twelfth where it curves forward along that rib for about 10 cm.; then it turns upward in the posterior axillary line to the level of the eighth rib. A musculocutaneous flap is raised, the twelfth rib resected, the eleventh sectioned at each end of its exposed part and the tenth cut only through its neck. The arteries in the corresponding intercostal spaces are ligated and cut and a large osteomuscular flap can then be raised, exposing the pleura and below this the diaphragm. The pleura is pushed forward off the vertebral column, aorta, esophagus and diaphragm. After the diaphragm is bared, it is split close to the neck of the twelfth rib near the esophageal orifice, and here the left inferior phrenic artery must be ligated before it is cut as its ends are likely to retract. After being split the diaphragm is retracted with the pleura and good exposure of the lower end of the esophagus is obtained.

For operations on the esophagus by the posterior mediastinal route, the side by which the better exposure is obtained still remains a matter

25. Lilienthal, Howard: Posterior Mediastinotomy, *Arch. Surg.* 6:274 (Jan.) 1923.

26. Grégoire, Raymond: Voie d'accès sur le segment cardio-œsophage permettant d'éviter la plèvre et le péritoine. (Voie thoraco-abdominale extra-séreuse), *J. de chir.* 21:673, 1923.

of the choice of the individual surgeon; most are agreed that the right side is better for operations in the region of the hilum and that the lower part of the thoracic portion of the esophagus is better approached from the left.

From the foregoing brief outline of the development of surgery of the esophagus, it can be seen that the viscus has become accessible throughout the whole length of the course. In the thorax two routes are available, the extrapleural and the transpleural. The abdominal part of the esophagus can be exposed through either the abdominal or the thoracic route.

LESIONS OF THE ESOPHAGUS

All lesions in the esophagus have a tendency to cause narrowing of the lumen, thus producing obstruction with its attendant symptoms. The esophagus, like any of the other hollow viscera in the body, may be obstructed by causes: (1) in the lumen, such as foreign bodies and tumors (polypi); (2) in the wall itself, such as cardiospasm, congenital stricture or stricture resulting chiefly from fibrosis in injury, inflammation or new growths—tumors, apart from fibrosis, may lead to narrowing—and (3) outside the wall, such as tumors, diverticula, aneurysms, enlarged lymph nodes and abscesses.

Treatment, whether or not it is surgical, is always directed toward relief from the obstruction. With regard to impacted foreign bodies, it is noticed that their removal has passed largely from the domain of surgery since the advent of the esophagoscope. Should operation be the only available means of relief, however, it would consist in exposure of the esophagus at the site of impaction and longitudinal incision through the wall over the foreign body followed by extraction with as little resultant trauma as possible. The edges of the esophageal wound would then be brought together, usually with two rows of sutures, the second inverting the first. Drainage must be provided for. Should the impacted foreign body be situated in the cardiac or lower thoracic part of the esophagus, it might be possible to extract it through a gastrotomy wound by digital manipulation and so avoid the risk entailed of opening the esophagus.

As mentioned, operation has been almost eliminated from the treatment for cardiospasm, and its place has been taken by the more conservative treatment of dilatation.

The stricture resulting from fibrosis following injury or inflammation (benign cicatricial stricture), when believed to be impermeable, has been treated by the plastic formation of an artificial esophagus which circumvents the stricture and reestablishes continuity between the mouth and stomach. In order that the surgical treatment of a carcinomatous stricture may be successful, resection of the growth itself is essential. Although subsequent end-to-end anastomosis may be attempted, it is

more usual to bridge the gap caused by the resection by some plastic procedure. Hence two series of operations for the relief of stricture have been attempted: esophagoplastic operation alone and resection with or without a plastic operation.

ESOPHAGOPLASTIC OPERATIONS

The types of plastic operations devised for the relief of benign cicatricial strictures which are believed to be impermeable, having as their object the formation of an artificial esophagus, have been many and various, and no tissue or viscus that would seem suitable has been neglected. Thus, skin, fascia, stomach and large and small intestines have all been used. Before the introduction of these operations, patients were usually subjected to gastrostomy, and there surgical treatment ended. Gastrostomy as a temporary measure is helpful, but as a permanent one it has many drawbacks and may become a veritable nuisance, particularly for a working man. The patient's food must always be specially prepared; the skin around the gastrostomy opening often becomes ulcerated and difficult to keep clean, and, what is even more exasperating to the patient, nothing has been done which will restore to him the joy of taking food by mouth and the power of deglutition for which he seems to crave and without which life seems to be intolerable. In spite of this unfortunate state to which gastrostomy may lead, many surgeons regard it with favor and publish statements to the effect that their patients are well satisfied with the results. Another fact which must be given just consideration is the youth of most of the patients suffering from benign stricture of the esophagus (many of them are actually children); to provide them only with a gastrostomy opening will limit their enjoyment of social intercourse and activity, and probably seriously jeopardize their chances of success in life. The realization of these drawbacks to gastrostomy was the factor which led to the introduction of esophagoplasty.

It may take months to complete the plastic operations, and the futility, as well as the lack of justification, of performing them in cases of carcinomatous stricture without primary resection of the growth itself has long been recognized. I shall describe the various types of esophagoplastic operations.

Skin.—In 1894, H. Bircher attempted extrathoracic esophagoplasty for carcinomatous stricture, using the skin of the anterior wall of the thorax and the neck. The first step was to make two vertical parallel incisions about from 7 to 8 cm. apart, slightly to the left of the median line and extending from the submaxillary region to the margin of the rib. The edges of the strip of skin were turned forward and brought together in the median line by interrupted sutures so that a tube lined by epidermis was formed. The edges of the skin of the incision on

both sides were undermined for 1 or 2 cm., pulled together and sutured over the tube of skin already formed. About six weeks later a gastrostomy opening was made and its edges connected with those of the lower opening of the tube of skin. Nine days later fluid nourishment was poured through the tube from above and it entered the stomach without trouble. Three days later the patient died of pulmonary embolism. At necropsy it was found that the sutures of the tube had given way in some places. The second patient died from pneumonia, and Bircher found that the anterior part of the tube of skin had separated for about 4 cm. and that from this opening the lumina of both stomach and tube could easily be reached. Bircher had intended to make a juncture between the upper end of the tube with the cervical part of the esophagus. He stated that although fluid food passed down the artificial esophagus with ease, he did not believe that solid food would, owing to the absence of peristalsis in the tube. Although Bircher's attempts to form a new esophagus were made in 1894, they were not published until 1907, by E. Bircher.²⁷ This procedure and its modifications, which seem to be the safest of all the methods devised for esophagoplasty, curiously enough seem to have been forsaken for a long time through the introduction of other much longer and more dangerous procedures, and have found favor again only during the last few years.

Payr,²⁸ in 1917, seems to have been the first to complete successfully Bircher's technic; the patient was a young man, aged 20.

In 1917, Esser²⁹ devised an ingenious method of forming a tube of skin to act as a new esophagus. He considered that in the formation of a tube according to Bircher's method there was likely to be too much tension on the skin and he found a method of avoiding this factor. He first performed a Witzel operation for gastrostomy. Then he made a transverse incision about 4 cm. long through the skin of the anterior wall of the thorax midway between the jugular notch and the gastrostomy opening slightly to the left of the sternum. After entrance to the subcutaneous tissues through the incision with a suitable instrument, he undermined the skin upward and outward to the level of the thyroid gland and downward to the gastrostomy opening. The thickest instrument was from 2.5 to 3 cm. in diameter. He then proceeded to line the tunnel with Thiersch skin grafts, so that when these had taken he

27. Bircher, Eugen: Ein Beitrag zur plastischen Bildung eines neuen Oesophagus, *Zentralbl. f. chir.* **34**:1479, 1907.

28. Payr: Fälle von antethorakalen Oesophagoplastik, *München. med. Wchnschr.* **64**:783, 1917.

29. Esser, J. F. S.: Sogennante total Oesophagoplastik aus Hautlappen nach Thiersch ohne Verwendung von Darmschlinge, *Deutsche Ztschr. f. Chir.* **142**:403, 1917.

had a tube lined by skin and formed in such a manner as to avoid tension. The technic of applying the grafts to the inside of the subcutaneous tunnel is interesting. He split a rubber drainage tube longitudinally and painted it with albumin (white of egg); when this was dry, he laid on it the Thiersch grafts, wound side outward, and turned the edges of the grafts into the longitudinal slit. The adhesion of the Thiersch grafts to the tube by the medium of the egg-white enabled the tube to be introduced into the tunnel with the grafts in position. Two graft-covered tubes were inserted, one into the upper part of the tunnel, the other into the lower part. Their approximated ends were connected by a core made of sterile wood. After ten days, the rubber tubes were removed and the upper and lower parts of the skin tube united by suture. In his first case, Esser had considerable difficulty in uniting the cervical portion of the esophagus with the upper end of the tube of skin because of the high position of the stricture and the consequent short length of the oral end of the esophagus. He managed, however, by closing the defect with skin flaps. He effected the juncture of the gastrostomy opening and the lower end of the tube of skin by constructing a sac from the abdominal wall to surround both orifices. The sac was made in the same way as the Bircher tube of skin. By this method a valvelike arrangement was made whereby he hoped to prevent the regurgitation of gastric contents (with their deleterious effects on the Thiersch grafts) into the skin tube, for the sac would have to become filled first and in filling would compress the anterior wall of the lower end of the skin tube against the posterior wall and so close the orifice. His first case was successful and at the time of writing he had begun a second case but had completed only the formation of the tube of skin by his Thiersch graft method.

In 1921, Fonio³⁰ suggested that the lower end of the tube of skin be joined directly to the wall of the stomach, the mucosa being sutured to the lower edge of the tube of skin followed by serous sutures inverting the wall of the stomach, as in a Senn gastrostomy. The soft tissues, then the skin, would be brought together and sutured over the anastomosis of the stomach and tube of skin.

Realizing the advantage of a seroserosus suture, Galpern,³¹ in 1925, sought to remedy this defect in the lower end of the skin tube by the use of omentum. He first made a transverse incision in the skin about 8 cm. long, midway between the xiphoid and the umbilicus, and undermined the skin above it, making a subcutaneous pocket from 5 to 6 cm. long. In this he placed omentum, which was extracted from

30. Fonio, A.: Ein Fall von antethorakalen Oesophagoplastik, Schweiz. med. Wchnschr. 51:865, 1921.

31. Galpern, E. J.: Eine neue Methode der Oesophagoplastik, Zentralbl. f. Chir. 52:182, 1925.

the abdomen. A week later, he made a tube of skin according to the method of Bircher, the lower edge being formed by the transverse incision, so that the lower 4 or 5 cm. was surrounded with omentum which had grown together with the subcutaneous tissues. In this way Galpern provided a serosal covering for the lower part of the skin tube, to which the stomach might then be united. He experimented on rabbits and dogs. In the former, all experiments were failures because the skin covering the pocket became mummified and unsuitable for the formation of a skin tube. By his experiments on dogs he was able to convince himself that the omentum grows together with the subcutaneous tissue and will take part in an anastomosis as serosa. He expressed the belief that heterogeneous omentum procured during laparotomy, for example, can be used with greater facility and with equally good results. His experiments were not completed when he made his report.

In 1922, von Engelbrecht³² reported a case of a girl, aged 15, on whom he performed anterior esophagoplasty for impermeable stricture. He successfully completed the artificial esophagus, although he had some trouble with the formation of fistula at the juncture of the skin tube and the esophagus above the gastrostomy opening and skin tube below.

In 1925, Rovsing³³ described a method which appeared to be a modification of that introduced by Bircher with which Rovsing appears to have been unfamiliar. Juncture of the lower end of the skin tube and the gastrostomy opening is effected in a manner similar to that in which Esser made the sac, except that the amount of skin used is just sufficient to form a tube continuous with the lower end of the skin tube above and surrounding the gastrostomy orifice below. An interesting modification which Rovsing introduced lay in his treatment of the aboral end of the esophagus after its division in the neck. Instead of closing it, which is the usual practice, he brought it out through a small incision in the left supraclavicular fossa, fixed it to the skin with silk and drained it with a tight rubber drain. In this way he avoided the possibility of mediastinitis which might ensue from the inefficient closure of the aboral end or from the giving way of the closing sutures because of tension resulting from secretion accumulating above the stricture. At this time he reported two successful cases, and in 1926, this number had increased to four, with a fifth which was incomplete.³⁴ Two of the patients were boys aged 5 and 9 years.

32. Von Engelbrecht, H.: Beitrag zur antethorakalen Oesophagoplastik, Beitr. z. klin. Chir. **126**:278, 1922.

33. Rovsing, Thorkild: Antethoracic Oesophagoplasty: A New Method, Ann. Surg. **81**:52, 1925.

34. Rovsing, Thorkild: The Technique of My Method of Antethoracic Oesophagoplasty. Surg. Gynec. Obst. **43**:781, 1926.

In 1926, Braizew³⁵ completed esophagoplasty on a girl, aged 12, by means of skin, although the procedure occupied nearly a year and necessitated many operations. His technic differed from the technics described in that he avoided the juncture of the skin tube with the gastrostomy opening by making a second opening in the stomach near the cardia. This allowed the temporary use of the first opening for feeding purposes and also reduced the length of the skin tube. The second opening was made by drawing up a cone of stomach into the abdominal wound and surrounding it with crossed muscle strips from the rectus abdominis, thus forming a sphincter. The functional result was good, the patient being able to swallow any kind of food.

Anterior Wall of the Stomach.—In 1901, Depage³⁶ by devising a new method of gastrostomy, paved the way for the later real esophagoplastic operations. He used a vertical flap from the anterior wall of the stomach with its base upward and close to the lesser curvature. By closing the stomach with a continuous suture and continuing this on to the upturned flap, he converted the latter into a tube which he found could be drawn upward through a parietal tunnel almost to the xiphoid process. In 1903,³⁷ he reported having used the method in six cases with satisfactory functional results.

In 1911, Hirsch³⁸ employed the same method but with the intention of replacing the lower part of the esophagus by the tube formed by the suturing of the edges of the flap. He made the longitudinal axis of the flap parallel to that of the stomach with the base toward the fundus, in this way ensuring a good blood supply from the branches of the left gastric and short gastric arteries. The lower end of the tube was fixed to the peritoneum to avoid kinking, and the tube itself was brought up onto the thorax subcutaneously. Jankovskis³⁹ quoted E. Hesse as having performed the Hirsch operation four times with two successful results. This is the only instance noted in the literature of the use of this operation on man. Jankovskis also pointed out that its disadvantage lies in the fact that the stomach considerably diminishes in size in cases of impermeable esophageal stricture.

35. Braizew, W. R.: Zur Frage der antethorakalen Dermato-Oesophagoplastik, Zentralbl. f. Chir. **53**:2010, 1926.

36. Depage, A.: Nouveau procédé pour la gastrostomie, J. de chir. et Ann. Soc. Belge de chir. **1**:715, 1901.

37. Depage, M.: Nouvelle méthode de gastrostomie, abstr. Presse méd. **19**:755, 1903.

38. Hirsch, Maximilian: Plastischer Ersatz des Oesophagus aus dem Magen, Zentralbl. f. Chir. **38**:1561, 1911.

39. Jankovskis, J.: L'oesophagoplastie totale; ses résultats fonctionnelles, J de chir. **25**:633, 1925.

Greater Curvature of the Stomach.—In 1905, Beck⁴⁰ started to improve gastrostomy by the formation of a plastic tube from the greater curvature of the stomach, with its base to the left, thus ensuring a good blood supply by means of the left gastro-epiploic artery. He cut a flap, and, by a continuation of the suture which closed the stomach on to the edges of the flap, brought them together and so formed a tube. Starting first with a small flap, he gradually extended the operation until most of the greater curvature was included in the flap. He then found that the tube was of such length that it could be brought upward on the surface of the thorax far enough to be united to the cervical portion of the esophagus. By measurements on the cadaver, he came to the conclusion that the operation was feasible on the human being. His experiments, which were briefly recorded in a journal of limited distribution, were not spread abroad in the general medical literature, and, consequently, the credit of having devised this form of esophagoplasty has mostly gone to Jianu,⁴¹ who, in 1912, apparently in ignorance of Beck's work, published similar experiments on dogs and on the cadaver and advised the use of the method for benign stricture in the human subject. After the formation of the tube, its base is sutured to the peritoneum in the upper part of the abdominal wound. A vertical median line incision is made in the skin of the thorax and the edges undermined. The tube is then drawn upward, laid in this subcutaneous path and the edges of skin sutured together over it. The edges of the end of the tube are sutured to those of a transverse incision at the upper end of the vertical one. Later, anastomosis can be made between the oral end of the transversely cut cervical portion of the esophagus and the upper end of the tube made from the greater curvatures.

Röpke,⁴² in 1921, was the first to use the Beck-Jianu type of esophagoplasty in operating on the human being. He performed the operation on a man with carcinoma of the esophagus, but did not do a resection. Instead of making a subcutaneous pathway for the artificial esophagus as did Jianu,⁴¹ he tunneled below the pectoral muscles. The gastric contents did not regurgitate. The case was successful apart from the fact that the carcinoma was not resected.

In 1913, Meyer⁴³ published a report of three cases in which the Beck-Jianu method of operation was successful. The first case was

40. Beck, Carl: Demonstration of Specimens Illustrating a Method of Formation of a Prethoracic Esophagus, *Illinois M. J.* 7:463, 1905; *Plastic Operations on the Stomach: An Experimental Study*, *Surg. Gynec. Obst.* 20:170, 1915.

41. Jianu, Amza: *Gastrostomie und Oesophagoplastik*, *Deutsche Ztschr. f. Chir.* 118:383, 1912.

42. Röpke, W.: *Ein neues Verfahren für die Gastrostomie und Oesophagoplastik*, *Zentralbl. f. Chir.* 39:1569, 1912.

43. Meyer, Willy: *Oesophagoplasty*, *Ann. Surg.* 58:289, 1913.

complicated by gangrene of the seromuscular coat of the uppermost extremity of the new esophagus. He believed this was due to the constricting action of the through-and-through sutures on the vessels, and formed the opinion that the mucosa alone should be sutured to the borders of the skin wound. In this case, Meyer had followed Röpke's method of leading the new esophagus through a subpectoral tunnel. Submuscular suppuration and perichondritis ensued. In his other two cases, he used Huelte's wire-stitching instrument for the closure of the longitudinal incision in the stomach; it has the great advantage that the stomach is not even opened. Meyer preferred the subcutaneous rather than the subpectoral placing of the Beck-Jianu tube because local infection is easier to deal with, and there is less risk of its spreading to the ribs or sternum. In another publication, Meyer⁴⁴ advised the intrathoracic use of the Beck-Jianu tube to replace the lower portion of an esophagus that had been resected for carcinoma.

In 1914, Jianu⁴⁵ reported the cases of the first two patients treated by this method. Both were cases of benign stricture, and the results were successful. He stated that it was feasible to perform the operation not only on a normal stomach, but also on one which might be adherent to the abdominal wall, as after gastrostomy.

In 1913, Enderlen and Hotz⁴⁶ reported their experimental work on esophagoplasty. They stated that their efforts to substitute a loop of small bowel or a Beck-Jianu tube for the esophagus uniformly resulted in gangrene, and that the mobilization of the proximal portion of the cervical esophagus resulted in failure because of necrosis of its end.

In 1919, Nicolaysen⁴⁷ published the report of an interesting case. A few years previously the patient had undergone a Wullstein and Roux⁴⁸ type of operation for esophageal stricture. The jejunal loop had necrosed, the operation thus being a failure. Nicolaysen then operated by the Beck-Jianu method, completing the new esophagus by a tube of skin. Complete success rewarded his efforts.

44. Meyer, Willy: Ein Vorschlag bezüglich der Gastrostomie und Oesophago-plastik nach Jianu-Röpke, *Zentralbl. f. Chir.* **40**:267, 1913.

45. Jianu, Amza: Ueber Oesophagoplastik, *Deutsche Ztschr. f. Chir.* **131**:397, 1914.

46. Enderlen and Hotz: Experimente zur Oesophaguschirurgie, *Zentralbl. f. Chir.* **40**:1175, 1913.

47. Nicolaysen, John: Ein Fall von gelungener Oesophagusplastik, *Zentralbl. f. Chir.* **46**:922, 1919.

48. Wullstein, L.: Ueber antethorakale Oesophago-Jejunostomie und Operationen nach gleichem Prinzip, *Deutsche med. Wchnschr.* **30**:734, 1904. Roux: L'oesophago-jéjunogastrostomose, nouvelle opération pour rétrécissement infranchissable de l'oesophage, *Semaine méd.* **27**:37, 1907.

In 1922, Lotheissen⁴⁹ reported four cases in which successful operations were performed by this method. In two of them the cervical portion of the esophagus was united directly with the Beck-Jianu tube, while in the remaining two this juncture had to be effected by the interposition of a tube of skin about 10 cm. long. In one of the latter cases, regurgitation of gastric contents caused erosion of the skin tube so that many minor plastic operations had to be performed for repair, the outcome finally being successful.

In 1926, Grigorjev⁵⁰ in a plastic operation, made a tube from the greater curvature of the stomach, constructed in such a manner as to open into the stomach near the pylorus, in this respect differing from the Beck-Jianu tube. It was brought up to the clavicle without tension. The functional result was poor: fluids would not pass into the stomach through the tube, and if introduced through a stomach tube, they regurgitated into the new esophagus. This was thought to be due to the resistance of the pyloric sphincter; a plastic operation was performed on this structure, but there was no improvement in function. The patient died after four months. Grigorjev considered this operation unsuitable and recommended the Wullstein-Roux type of esophagoplasty.

Whole Stomach (Antiperistaltic).—In 1913, von Fink⁵¹ devised a method of operating on a patient who had a carcinoma of the cardia and lower end of the esophagus. At operation he found the cardia forming a stiff funnel and adherent to the liver. He mobilized the remainder of the stomach and first part of the duodenum, cut through the juncture of the first and second parts of the duodenum and closed the distal end. He then brought up the stomach over the left margin of the ribs onto the anterior thoracic wall subcutaneously, although the extent to which he did this was naturally limited by the fixation of the cardia. The opening of the duodenum reached to about the level of the nipple. Posterior gastro-enterostomy was then performed. Later, the cervical portion of the esophagus was united to the duodenal opening. After a few days, blood-stained fluid flowed from the abdominal wound. The fluid increased in amount, and the patient became weaker and died. By this operation von Fink established in his own mind the usefulness of the stomach and duodenum as material for esophagoplasty.

49. Lotheissen, G.: Zur Behandlung der Speiseröhrenstrikturen, Zentralbl. f. Chir. 40:1969, 1913; Ueber plastischen Ersatz der Speiseröhre insbesondere aus dem Magen, Beitr. z. klin. Chir. 126:490, 1922.

50. Grigorjev, A.: Bildung einer künstlichen Speiseröhre nach Halpern, abstr. Zentralorg. f. d. ges. Chir. 37:104, 1927.

51. Von Fink, Franz: Ueber plastischen Ersatz der Speiseröhre, Zentralbl. f. Chir. 40:545, 1913.

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Whole Stomach (Isoperistaltic).—In 1920, Kirschner⁵² introduced a new method of esophagoplasty, in which, like von Fink,⁵¹ he used the whole stomach. After ligating and dividing the left gastric, left gastro-epiploic and short gastric arteries, he mobilized the whole stomach by cutting through the gastrocolic and gastrohepatic ligaments. He then cut through the stomach about 4 cm. below the cardia and, after making an anastomosis between the cardiac stump and the jejunum, he drew up the stomach subcutaneously, cardiac end first, in front of the wall of the chest. He thus arranged the stomach in an isoperistaltic way, because he feared the effect of antiperistalsis which might cause trouble in the von Fink type of operation. Later, the cervical portion of the esophagus was to be anastomosed to the cardiac end of the stomach. Kirschner reported one case in which the operation was completed with a successful result, which, however, took twenty-seven months to attain, the chief difficulty being the contraction of the cervical esophagostomy opening, which required many minor plastic operations. His second patient lived only a month, and died from abscess of the lung. At necropsy an ulcer was found in the displaced stomach at the level of the third rib; it had perforated into the pectoralis major muscle.

In 1921, Kümmell⁵³ performed esophagoplasty, using Kirschner's method in three cases of impermeable stenosis due to cardiospasm, benign stricture and inoperable carcinoma, respectively. All three patients died soon after the operation. In two of them, Kümmell did not anastomose the cardiac end of the esophagus with the small intestine. In each of them, the accumulation of secretion above the closing ligature resulted in rupture with peritonitis. At necropsy, there were no signs of impairment of nutrition of the wall of the stomach in any of the cases.

In regard to the mobilization of the stomach, the work of Miller and Andrus,⁵⁴ in 1923, is of importance. They found that in nineteen dogs in which the left gastric and short gastric arteries, as well as the anastomotic branches from the phrenic arteries near the cardia were ligated, only one showed any alteration in the viability of the stomach; a definite necrosis of a limited portion of the fundus took place. On the other hand, if one goes a step further and divides the left gastro-epiploic artery (as Kirschner did), one finds that in dogs at least two thirds of the stomachs so treated show an area of necrosis on the

52. Kirschner: Ein neues Verfahren der Oesophagoplastik, Arch. f. klin. Chir. **114**:606, 1920.

53. Kümmell, Hermann: Zur Operation des Kardiospasmus und des Oesophaguscarcinoms, Arch. f. klin. Chir. **117**:193, 1921.

54. Miller, R. T., Jr., and Andrus, W. D. W.: Experimental Surgery of the Thoracic Esophagus, Bull. Johns Hopkins Hosp. **34**:109, 1923.

fundus from 3 to 4 cm. in diameter, involving the entire thickness of the wall and resulting in acute perforating ulcer. Such a lesion was found in Kirschner's⁵² second case. In view of their experience, Miller and Andrus considered Kirschner's method of mobilizing the stomach a risky procedure.

In 1926, Wajgiel,⁵⁵ working on dogs and cadavers, made injections into the stomachs after the ligation of the left gastric, short gastric and left gastro-epiploic arteries. He found that the fundus of a stomach, the blood supply of which had been treated in this manner, was not filled with the injection mass. This corroborates the observations of Miller and Andrus.

Jejunum.—Wullstein,⁵⁶ in 1904, was the first to utilize the jejunum for esophagoplastic work; he performed his experiments on the cadaver. He resected about 15 cm. of jejunum taken from the intestine a short distance (about 30 cm.) below the duodenojejunal flexure. After the reestablishment of the continuity of the bowel by end-to-end or lateral anastomosis, he pulled up the resected jejunal loop with its attached mesentery through the transverse mesocolon and greater omentum and anastomosed the aboral end to the anterior surface of the stomach. The oral end of the loop was then drawn up onto the anterior thoracic wall and sutured to the thoracic musculature along the left border of the sternum; over the loop of intestine so fixed he sutured the skin flap made with its base to the left prior to the opening of the peritoneal cavity. The anterior circumference of the end of the jejunal loop was sutured to the skin laid over it. The next step was to make a tube of skin in a similar manner to that of Bircher and to join it below to the upper end of the jejunum and above to the oral end of the divided cervical portion of the esophagus.

In 1907, Roux⁵⁷ performed his famous successful operation of esophagojejunogastrostomy on a child suffering from intractable benign esophageal stricture. In reality this was a modification of Wullstein's method. His results with gastrostomy in benign stricture had been poor, and he decided to attempt to form a new esophagus with the aid of the small intestine. He took the jejunum because of the regularities of the arteries supplying it and the ease with which they are recognized. He first resected a loop of the upper portion of the jejunum of a length calculated to reach almost to the pharynx. Toward its oral end he ligated and cut the vascular stems of the arcades and then divided the mesentery.

55. Wajgiel, Eugenjusz: Experimentelle Untersuchungen über die Gefäßversorgung des Magens insbesondere mit Rücksicht auf die Operation der vollständigen Oesophagoplastik nach Kirschner, abstr. Zentralorg. f. d. ges. Chir. **36**:34, 1926-1927.

56. Wullstein (footnote 48, first reference).

57. Roux (footnote 48, second reference).

At its aboral end, he conserved the mesentery containing one or more arterial stems, and thus obtained a length of intestine supplied with blood through its mesenteric pedicle. Then followed the reestablishment of the continuity of the intestine by a button for intestinal anastomosis. The resected loop was drawn up in front of the transverse colon and the aboral end implanted in the stomach close to the lesser curvature, care being taken not to compress the transverse colon. By means of Richelot forceps, Roux undermined the skin of the thorax just to the left of the sternum as far upward as the manubrium, where they came out through a transverse incision. By opening the forceps and giving them a to-and-fro movement, he made a tunnel through which the jejunum was easily drawn, and the circumference of the end of the loop was sutured to the edges of the wound in the skin. The peritoneum was closed. After the wounds had healed, the subcutaneous intestinal loop could be seen to contract actively at intervals. Roux was later going to join the cervical portion of the esophagus to the upper end of the jejunal loop and so complete that which he set out to do.

Thus, to Roux belongs the credit of proving the feasibility of making a new esophagus from the intestine in human beings. It infused new enthusiasm into the minds of many who had hitherto believed such surgical success to be impossible, and this was reflected in the increased number of case reports of attempted esophagoplasty which began to appear in the literature. Judging from the literature, of all types of esophagoplasty the Wullstein-Roux method has proved the most popular. The juncture of the cervical portion of the esophagus with the jejunal loop sometimes is direct as devised by Roux, and sometimes by skin esophagoplasty according to Wullstein.

In 1908, Herzen⁵⁸ performed a Roux operation on a patient with carcinoma. Death followed sixteen days afterward. Herzen was not satisfied with Roux's technic and sought to change it somewhat, the chief modification being the passing of the jejunal loop through the transverse mesocolon and gastrocolic omentum so as to shorten it and to avoid the possibility of compression of the transverse colon. Later, he completed the operation in two cases with success. The first was that of a man with carcinoma of the esophagus, who was shown at the Seventh Russian Surgical Congress, at which time he enjoyed good health. The other was that of a girl, aged 20, who had stricture which resulted from swallowing sulphuric acid. Herzen mentioned that in this case intestinal peristalsis showed itself in the jejunal loop after each new mouthful of food. His modification of shortening the path of the jejunal loop by passing it through slits in the transverse mesocolon and

58. Herzen, P.: Eine Modification der Rouxischen Oesophagojejunogastrostomie, *Zentralbl. f. Chir.* 35:219, 1908.

gastrocolic omentum had already been suggested by Wullstein in 1904. In 1908, Wullstein⁵⁹ drew attention to the similarity of his method to that of Bircher and Roux.

In 1911, Lexer⁶⁰ performed a Roux operation for carcinoma of the esophagus. Gangrene of the subcutaneous loop of intestine ensued. He performed the Wullstein operation in another case with success. Lexer, watching this case, made the important observation that the absence of peristalsis in the section containing the skin tube of the artificial esophagus did not have an adverse effect on the ingestion of food. Thus, Bircher's doubts as to the ability of such an esophagus to allow the passage of solid food were settled. It was a most interesting observation from the physiologic standpoint as it proved that the esophagus itself plays a small part in deglutition, and that the descent of the food bolus is due to the impetus given to it by the contraction of the pharyngeal muscles.

Since this time many surgeons have reported one or more cases in which this type of operation was performed with varying degrees of success. The list is so large that only references will be given: Frangenheim,⁶¹ Heyrovsky,⁶² Blauel,⁶³ Rehn,⁶⁴ Sýring,⁶⁵ Axhausen,⁶⁶ Bornhaupt,⁶⁷ Hirschmann,⁶⁸ Fromme,⁶⁹ von Hacker,⁷⁰ Ranzi,⁷¹ Peter-

59. Wullstein, L.: Zur plastischen Bildung eines neuen Oesophagus, *Zentralbl. f. Chir.* **35**:222, 1908.

60. Lexer, E.: Vollständiger Ersatz der Speiseröhre, München. med. Wchnschr. **58**:1548, 1911.

61. Frangenheim, Paul: Zur Frage der Oesophagus plastik, *Arch. f. klin. Chir.* **95**:684, 1911.

62. Heyrovsky, Hans: *Wien. klin. Wchnschr.* **27**:89, 1914.

63. Blauel, K.: Zur totalen Oesophagus plastik, *Verhandl. d. deutsch. Gesellsch. f. Chir.* **43**:119, 1914.

64. Rehn, Eduard: *Oesophagus-Chirurgie*, Jena, Gustav Fischer, 1914, p. 169.

65. Sýring: Klinisches und Experimentelles zur Oesophagoplastik, *Deutsche Ztschr. f. Chir.* **128**:260, 1914.

66. Axhausen, G.: Zur totalen Oesophagoplastik, *Berl. klin. Wchnschr.* **1**:54, 1916; Die Technik der antethoracalen Totalplastik der Speiseröhre, *Beitr. z. klin. Chir.* **120**:163, 1920; Zur technik der Oesophagoplastik, *Arch. f. klin. Chir.* **139**:645, 1926.

67. Bornhaupt, Leo: Zwei geheilte Fälle von totaler Oesophagoplastik, *Arch. f. klin. Chir.* **111**:315, 1919.

68. Hirschmann, Carl: Die Bedeutung und Technik des antethorakalen Speiseröhrenersatzes bei den impermeablen Strikturen, *Therap. d. Gegenw.* **60**:368, 1919.

69. Fromme, Albert: Ueber totale Oesophagoplastik, *Beitr. z. klin. Chir.* **115**:222, 1919.

70. Von Hacker, Viktor: Zur antethorakalen Oesophagoplastik mittels Haut-Darmschlauchbildung, *Zentralbl. f. Chir.* **46**:1, 1919.

71. Ranzi, E.: Ueber totale Oesophagoplastik, *Wien. klin. Wchnschr.* **32**:247, 1919.

sen,⁷² Kreuter,⁷³ Madlener,⁷⁴ Bohmansson,⁷⁵ Hinz,⁷⁶ Lotheissen,⁴⁹ Frangenheim,⁷⁷ Nigol,⁷⁸ Király,⁷⁹ Bakay,⁸⁰ Strahle,⁸¹ Flechtenmacher,⁸² Riesenkampff,⁸³ Jankovskis,³⁹ Sebestýen,⁸⁴ Denk,⁸⁵ Pokotilo⁸⁶ and Albrecht.⁸⁷

Colon (Isoperistaltic).—In 1911, Kelling,⁸⁸ impressed by Lexer's⁶⁰ successful case which had just been reported, decided to attempt a similar operation, and chose as his patient a man, aged 45 with an ulcerating esophageal carcinoma. When the abdomen was opened he noticed the shortness of the mesentery of the small intestine as compared to that of the transverse colon, and therefore decided to try the suitability of this part of the large intestine for esophagoplasty. He resected a large piece of the transverse colon, reestablished the continuity by end-to-end anastomosis, closed the right end of the resected portion and anastomosed its left aboral end to the anterior surface of

72. Petersen: Demonstration eines Falles von antethorakaler Oesophagusplastik bei kongenitaler Oesophagusstenose, Zentralbl. f. Chir. **48**:520, 1921.

73. Kreuter, E.: Zur Technik der antethorakalen Oesophagoplastik, Zentralbl. f. Chir. **47**:1266, 1920.

74. Madlener, Max: Ueber den Ersatz der Speiseröhre durch antethorakale Schlauchbildung, Deutsche Ztschr. f. Chir. **155**:410, 1920.

75. Bohmansson, Gösta: Antethoracal Oesophageal Plastic Operation, Acta chir. Scandinav. **53**:91, 1921.

76. Hinz, R.: Zur präthorakalen Oesophagusplastik, Deutsche med. Wchnschr. **47**:1089, 1921.

77. Frangenheim, Paul: Oesophagoplastik Methodik und Erfolge, München. med. Wchnschr. **69**:303, 1922.

78. Nigol, Karl: Dermoentero oesophagoplastica antethoracalis, abstr. Zentralorg. f. d. ges. Chir. **26**:309, 1924.

79. Király, J.: Drei Fälle extrathorakaler Oesophagoplastik, abstr. Zentralorg. f. d. ges. Chir. **32**:26, 1925.

80. Bakay, L.: Zwei Fälle von extrathorakale Oesophagoplastik, abstr. Zentralorg. f. d. ges. Chir. **32**:26, 1925.

81. Strahle, Lennart: Ein Fall von antethorakaler Oesophagusplastik, Acta chir. Scandinav. **58**:1, 1925.

82. Flechtenmacher, C., Jr.: Zur totalen antethorakalen Oesophagoplastik, Wien. med. Wchnschr. **75**:2590, 1925.

83. Riesenkampff, Otto: Ein Fall von totaler Oesophagoplastik, Deutsche Ztschr. f. Chir. **193**:116, 1925.

84. Sebestýen, Julius: Ueber Mechanismus und Wert der künstlichen Speiseröhre, Deutsche Ztschr. f. Chir. **193**:238, 1925.

85. Denk, W.: Ueber den Ersatz der Speiseröhre durch antethorakale Plastik, Wien. med. Wchnschr. **76**:582, 1926.

86. Pokotilo, V.: Ein Fall von antethorakaler Oesophagusplastik nach Roux, 3 Jahre lang verfolgt, abstr. Zentralorg. f. d. ges. Chir. **37**:333, 1927.

87. Albrecht, P.: Dermato-Jejunoplastik des Oesophagus, Wien. med. Wchnschr. **76**:1121, 1926.

88. Kelling, G. E.: Oesophagoplastik mit Hilfe der Querkolon, Zentralbl. f. Chir. **38**:1209, 1911.

the stomach near the fundus. The mesentery of the resected portion of the colon was preserved completely only at its left end and thus contained the left colic artery. A Kader type of gastrostomy was performed. The colon was drawn up onto the anterior thoracic wall, the skin of which was incised and undermined to receive it. The colon was laid in the subcutaneous channel and the skin sutured over it. The blind end of the colon was sutured to the upper part of the skin wound. The patient was nourished through the gastrostomy opening for a few days, and then the blind end of the colon was opened and the mucous membrane sutured to the skin. About a month after the first operation, the esophagus was brought out of the neck, and an attempt was made to bridge the gap between the esophageal fistula and the upper end of the colon. The patient collapsed and died when everything seemed to be going well.

Colon (Antiperistaltic).—In 1911 also, Vulliet⁸⁹ devised an operation similar to that of Kelling, but performed it only on the cadaver. The point of difference between the two methods is that Vulliet preserved the mesenteric pedicle at the right (oral) end of the resected intestine, and he anastomosed this end to the stomach, drawing the left (aboral) end up onto the chest. Thus, his arrangement of the resected portion of the colon was antiperistaltic. This did not worry Vulliet because of the observations of Lexer and Frangenheim which seemed to show that the peristalsis in such an excluded loop of intestine was hardly worth consideration.

The reports in the literature on esophagoplastic operations in which an excluded portion of the transverse colon was used have been few, and in those in which full reports are given the Kelling type of operation has been most commonly performed.

Von Hacker,⁹⁰ Fonio,⁹⁰ Lundblad,⁹¹ Ritter⁹² and Lotheissen⁴⁹ have all reported cases.

In 1923, Roith⁹³ devised a new one-stage method of esophagoplasty, using a part of the transverse colon and the cecum and ascending colon. He performed his operation on a man on whom gastrostomy had been performed for stricture of the esophagus. At the end of seventeen

89. Vulliet, H.: De l'oesophagoplastie et des diverses modifications, *Semaine méd.* **31**:529, 1911.

90. Von Hacker: Ueber Oesophagoplastik im allgemeinen und über den Ersatz der Speiseröhre durch antethorakale Haut-Dickdarmschlauchbildung im besondern, *Arch. f. klin. Chir.* **105**:973, 1914.

91. Lundblad, Olaf: Ueber antethoracale Oesophagoplastik, *Acta chir. Scandinav.* **53**:535, 1921.

92. Ritter: Diskussion, *Zentralbl. f. Chir.* **45**:521, 1921.

93. Roith, Otto: Die einzeitige antethorakale Oesophagoplastik aus dem Dickdarm, *Deutsche Ztschr. f. Chir.* **183**:419, 1923-1924.

days the patient was well enough to go home; the gastrostomy opening had closed. The patient fared well for three years, and then died of an intercurrent disease. Roith's procedure was as follows:

A large abdominal incision was made from the xiphoid process downward, at first vertically, then diagonally through the right rectus, as a good exposure is necessary. The cecum was loosened, the parietal peritoneum cut lateral to the ascending colon and this portion of intestine freed. The ileum near the ileocecal valve was cut through and both ends closed blindly. Transverse section was made of the middle of the transverse colon with blind closure of both ends, ileocolostomy by lateral anastomosis between the closed ends of the proximal ileum and the distal colon, and anastomosis between the aboral end of the excluded colon and the upper part of the anterior wall of the stomach. The cecal end of the colon was drawn up into the anterior thoracic wall subcutaneously to the neighborhood of the left clavicle where, after exposure of the cervical portion of the esophagus, anastomosis was made laterally by interrupted sutures to the cecum. This completed the one-stage esophagoplasty.

Comment.—Up to the end of 1921, Lotheissen⁴⁹ reviewed eighty-nine cases reported in the literature in which esophagoplasty for the relief of benign stricture had been performed by various methods. Forty-five of these operations were complete and 44 were incomplete. By the end of 1923, this number had been increased to 101 (von Hacker⁷⁰ and Lotheissen), with 50 complete and 51 incomplete. In 1926, Denk⁸⁵ added 19 complete cases from the literature to this list. He omitted, however, the cases of Sebestýen⁸⁴ (6 complete and 4 incomplete), Flechtenmacher⁸² (1 incomplete) and Jankovskis³⁹ (4 complete and 1 incomplete), and since he wrote, the reports of Perthes,⁹⁴ Braizew³⁵ and Albrecht⁸⁷ have appeared, each of whom completed 1 case, of Grigorjev⁵⁰ and Pokotilo⁸⁶ whose cases were incomplete, and of Rovsing⁹⁵ (2 complete and 1 incomplete). These additions (a total of 24 cases) are the result of a search in the literature up to the end of 1927, and make the total number of recorded esophagoplastic operations for benign stricture 144, of which 84 have been completed, with 60 incomplete. Death, sometimes from intercurrent diseases but usually resulting from the operative procedures, has been the most common reason for incompleteness: in the list compiled by von Hacker and Lotheissen it accounted for 25 of the incomplete cases, while in my additional 9 incomplete cases reviewed from the literature there were 5 deaths. The total mortality amounts to 20.8 per cent.

94. Perthes: Plastischer Ersatz der nach Laugenverätzung verschlossenen Speiseröhre (Krankenvorstellung), München. med. Wchnschr. 73:1465, 1926.

95. Rovsing (footnotes 33 and 34).

The case reports show an overwhelming preponderance of jejunoplasty by means of skin over the other types of jejunoplasty. This is particularly noticeable in the most recent cases: for example, in my collection of 24 cases. Only those of Rovsing,⁵³ Braizew⁵⁴ and Grigorjev⁵⁰ were done by other methods, leaving 18 which were performed by the Wullstein-Roux-Herzen type of operation.

It can be seen from the foregoing account of the esophagoplastic procedures that in a case of impermeable stricture the surgeon has the choice of several types of operation. They may be divided into two groups: those in which an abdominal viscus is used (beyond simple gastrostomy) and those in which the entire antethoracic esophagus is made from the skin of the wall of the chest.

The first group suffers from two disadvantages which are common to all types of operation belonging to it, whether the stomach, jejunum or colon is used. They are the risks of gangrene of the antethoracically transposed viscus due to insufficiency of, or interference with, its blood supply, and peritonitis. Although the latter is usually successfully guarded against by the adoption of present-day methods of surgical technic, the former must always remain a much more serious risk since it is dependent on several factors.

The disadvantages of jejunoesophagoplasty as performed by Roux are at once apparent. The loop of jejunum was so long that its blood supply could not be otherwise than poor. Moreover, by bringing up the loop in front of the transverse colon, the mesenteric pedicle was twisted, and there was risk of compression of the colon by it. Herzen corrected these faults by his modification of bringing up the jejunal loop through an incision in the mesocolon, thereby passing it behind the transverse colon. Hirschmann⁵⁶ suggested another improvement by making the skin tube so that its lower end is at the level of the xiphoid process, thus further shortening the length of the jejunal loop necessary for this operation, ensuring a much better blood supply and preventing the blind saclike dilatations near its juncture with the stomach which have sometimes given cause for resection.

Kirschner's⁵² method has the advantage that, with the exception of the anastomosis of the cervical portion of the esophagus with the stomach, the whole operation is done in one stage. It presents two difficulties, however: the anastomosis of the cardiac end of the esophagus (or the remaining cardiac part of the stomach) with the small intestine and the transposition under the skin of such a large viscus. The work of Miller and Andrus,⁵⁴ and later that of Wajgiel,⁵⁵ and the occurrence of a perforating gastric ulcer in one of Kirschner's cases would seem to indicate that the blood supply of such a mobilized

⁵⁶ Hirschmann, Carl: *Komplikationen bei der totalen Oesophagoplastik, Ihre Beseitigung und Verhütung; zugleich ein Beitrag zur Verwendung der "Epithaleinlage,"* Arch. f. klin. Chir. **122**:553, 1922.

stomach may, in a fair percentage of cases, prove to be so inadequate as to prevent the adoption of this type of esophagoplasty in preference to others.

Next to jejuno-esophagoplasty the method of Beck and Jianu has won most favor. Its disadvantages lie in the long suture line and in the production of acid and pepsin by means of the mucous membrane, the corrosive effect of which may seriously compromise healing. Most cases in which this method was used seem to have been successful in spite of the doubt cast on it by the experiments of Enderlen and Hotz, who found gangrene of the tube formed from the stomach in every case. Meyer and Lotheissen both regard this method as the best type of esophagoplasty.

In the Kelling and Vulliet type of operation, it is thought that the risk of peritonitis is considerable because of the virulence of the organisms usually found in this part of the bowel. There is also to be considered the difficulty of bringing up the colon subcutaneously, owing to its bulk. In these cases there is a tendency for food to collect and remain for some time on the lower part of the transposed loop before it passes into the stomach; this may affect the comfort of the patient.

In this group all the acids of the viscera are capable of peristaltic movement and may be transposed in either an isoperistaltic or an anti-peristaltic way. If in the former, then peristalsis, although usually it does not greatly help the functional results, at least is not detrimental to it. When the viscus is placed in an antiperistaltic manner, one would expect that peristalsis would adversely affect the function of the new esophagus. Under these circumstances, however, it behaves in such a paradoxical way that it seems impossible to foretell the result. Sýring arranged his jejunal loop antiperistaltically, and peristalsis, by causing a copious regurgitation of gastric juice, led to complete failure of the operation. On the other hand, Jankovskis performed a similar type of operation, and had no trouble whatsoever from this source.

In the second group fall the method of skin esophagoplasty of Bircher⁹⁷ and its modifications. These have a great advantage over the methods in the first group in that the only intra-abdominal operation necessary is simple gastrostomy, which in many cases has already been done as a palliative measure some time before it was decided to undertake the formation of an antethoracic esophagus, thus rendering any subsequent intra-abdominal procedure increasingly difficult because of adhesions. It has been realized that peristaltic action in an artificial esophagus is unnecessary; the cases of Torek⁹⁷ and of Eggers⁹⁸ are

97. Torek, F.: The First Successful Case of Resection of the Thoracic Portion of the Oesophagus for Carcinoma, *Surg. Gynec. Obst.* **16**:614, 1913.

98. Eggers, Carl: Resection of the Thoracic Portion of the Esophagus for Carcinoma: Report of a Successful Case, *Arch. Surg.* **10**:361 (Jan.) 1925.

proof of this. The formation of the tube of skin in males is likely to be difficult because of the tightness of the anterior thoracic skin, but tension can usually be relieved by means of suitably placed incisions. Judging from the literature, the least difficult and most successful part of any total antethoracic esophagoplasty is the formation of the skin tube.

Common to both groups are the difficulties that accompany the esophagostomy. There is often a marked tendency to stenosis. This should be overcome by the passage of bougies or by small plastic operations before anastomosis with the upper end of the skin tube is attempted. Some authors advise the direct union of the esophagus with the upper edge of the skin tube; others, that it should be united first with the skin of the neck and afterward the two orifices enclosed by a small tube of skin. The flow of saliva from the esophagostomy opening generally retards healing at this point. Some of the earlier workers were content to make only partial division of the esophagus and to unite the cut edges to the skin. This practice has been superseded by transection, on the grounds that by the former method food gained access to the culdesac above the stricture, resulting in stagnation and infection.

At the lower end of the skin tube the corrosive effect of the regurgitated gastric juice may retard healing at its juncture with a transposed abdominal viscus or the gastrostomy, causing fistula and necessitating many minor plastic operations.

Although many successful attempts have been made to form an artificial esophagus by antethoracic esophagoplasty, the surgeon who undertakes the operation should realize that he accepts a grave responsibility. It takes months to complete the procedure, the mortality is not low and success is far from being assured even if death does not occur. The avoidance of the necessity of the operation depends largely on a proper understanding of the term impermeable.

It has been known for many years that a swallowed silk thread will often worm its way through a stricture through which the smallest bougie cannot hope to penetrate. This fact formed the basis of von Hacker's⁹⁹ successful "sondierung ohne Ende" method of treating benign stricture. The lower end of the silk thread is drawn out of a gastrostomy opening, while a rubber tube is attached to the upper end, which is drawn downward through the stricture by pulling on the lower end of the thread. The upper end of the rubber tube is in turn attached to one of greater diameter, and this is next drawn down through

99. Von Hacker: Zur Behandlung tiefsitzender Narbenstricturen der Speiseröhre durch Sondierung ohne Ende nach temporärer Gastrostomie Oesophagostomie mit Bemerkungen über die Verwendung ausgezogener Drains zur Drainage ohne Ende. Wien. klin. Wchnschr. 7:455 and 480, 1894.

the stricture. By a continuation of this process, rubber tubes of gradually increasing diameters can be used to dilate the stricture to the required size. This method was modified by Dunham¹⁰⁰ who made use of metal sounds instead of rubber tubes. Mixer¹⁰¹ went a step further and introduced a modification of Dunham's technic which abolished the necessity of gastrostomy. He conceived the idea of using a silk thread which had passed through the stomach into the intestine, far enough to admit of its being drawn taut, as a guide for passing dilating sounds through the stricture. H. S. Plummer¹⁰² recognized the value of this method and introduced it into the Mayo Clinic where it is now carried on successfully by Vinson.¹⁰³ Many of Vinson's patients who have had gastrostomy performed for "impermeable" stricture, and others who, according to the roentgenologist, had complete occlusion, have swallowed a thread and it passed through the stricture, in spite of the fact that even the smallest sound failed to pass. He has not failed to dilate successfully in any such case. Reports in the literature show that many of these plastic procedures have been undertaken simply because the smallest bougies could not be passed through the stricture, and in view of the foregoing facts it would seem that many patients have been submitted unjustifiably to operations of long duration and considerable risk. No doubt there are rare cases in which anatomic impermeability occurs, and the lumen is completely occluded or at any rate obliterated to such an extent that all efforts to get a silk thread to pass through the stricture are of no avail. On the other hand, it should be recognized that in almost all severe cases the impermeability is only clinical and not anatomic, and can be satisfactorily treated by the well tried and successful method which has been described.

If a stricture finally becomes anatomically impermeable, it means that the stricture must have passed through the stage of clinical impermeability, at which time it was either neglected or wrong, or insufficient treatment was instituted. During its passage from clinical to anatomic impermeability, gastrostomy must have been performed; otherwise, the patient would have died from starvation. Hence, all patients who have an anatomically impermeable, benign, cicatricial stricture have been submitted also to gastrostomy. The question of further surgical intervention by the formation of an artificial esophagus now arises and

100. Dunham, Theodore: *New Instruments for the Treatment of Oesophageal Stricture*, *Ann. Surg.* **37**:350, 1903.

101. Mixer, S. J.: *Symposium on the Surgery of the Oesophagus, from the Standpoint of the General Surgeon*, *Tr. Am. Laryngol. A.* **31**:342, 1909.

102. Plummer, H. S.: *The Value of a Silk Thread as a Guide in Esophageal Technic*, *Surg. Gynec. Obst.* **10**:519, 1910.

103. Vinson, P. P.: *Personal communication to the author.*

is dependent on the efficiency of the gastrostomy. Should the patient be satisfied with this, nothing further need be done. On the other hand, should the gastrostomy prove inefficient and bring unbearable discomfort in its train, then antethoracic esophagoplasty is justifiable, provided that the risks and uncertainty of success are pointed out to the patient and he is willing to allow the surgeon to operate on the chance of success, which, if achieved, will allow him to take his place once again as a normal person.

Here a plea is made for the prevention of the progression of benign cicatricial stricture to either clinical or anatomic impermeability. So often the histories of patients suffering with this condition are stories of neglect, on the part either of the patient or of one or more physicians. Rutherford Morison's aphorism "Once a stricture, always a stricture" is as true of the esophagus as it is of the urethra, and if such patients were told this and were impressed with the likelihood that the stricture might become impermeable if not treated properly, there is no doubt that their negligence, often the outcome of ignorance, would be largely prevented. Thus, regular systematic dilatation could be undertaken and started shortly after the onset of the affliction. In this way cases of impermeable stricture would be reduced considerably or might be abolished altogether, although some authors hold the opinion that in rare cases the progression of a stricture to impermeability apparently cannot be prevented.

RESECTION WITH OR WITHOUT ACCOMPANYING PLASTIC OPERATIONS

The goal for which surgery is ever striving in esophageal work is successful resection for carcinoma. The difficulties in obtaining successful results have been discussed. They are as yet far from being surmounted with any degree of regularity. Judging from the literature, it would seem that every method which ingenuity can invent has been practiced for the purpose of reestablishing the continuity of the esophagus after resection either in the dog (the animal most frequently used for experimental esophageal surgery) or in man.

Cervical Portion.—The earliest reports concerning resection of the cervical portion of the esophagus are those of Billroth¹⁰⁴ and Czerny.¹⁰⁵

Billroth,¹⁰⁴ in 1871, was the first to turn his attention to resection of the esophagus, with extirpation of carcinoma as his ultimate object. He performed the operations on dogs. After exposing the esophagus, he freed it from the surrounding connective tissue, resected about 1.5 cm.

104. Billroth, T.: Ueber die Resection des Oesophagus, Arch. f. klin. Chir. 13:65, 1871.

105. Czerny, quoted by von Hacker: Arch. f. klin. Chir. 87:257, 1908.

and sutured the cut ends together. The first dog died in five days from a phlegmon of the neck. The second dog fared better; a fistula formed which discharged for several months but finally healed, and the dog lived in health until it was killed.

In 1877, Czerny,¹⁰⁶ one of Billroth's pupils, was the first to extirpate successfully the cervical part of the esophagus for carcinoma in a human being. He made the usual incision along the anterior border of the left sternomastoid and removed the portion of the esophagus from just below the pharynx to below the thyroid gland, thus being well clear of the tumor above and below; in all, about 6 cm. of the esophagus was removed. The distal end of the esophagus was stitched into the lower part of the skin wound, and the patient was fed by tube through the esophagostomy opening. She died fifteen months after the operation from recurrence.

In 1884, Mikulicz¹⁰⁶ went a step further; he followed resection of a cervical esophageal carcinoma with plastic repair of the fistula resulting from the operation. Four months after the first operation, he cut out the fistula with its surrounding skin, and on each side cut a small flap of skin with its base medially. He turned these flaps inward so that the epidermis was inside, and sutured their edges together. The skin lateral to the flaps was drawn together over them by means of silver wire sutures. The wound healed by first intention, and after ten days the patient was able to swallow solid food. Death from recurrence occurred sixteen months after resection.

Mikulicz' plastic operation was an afterthought, and von Hacker,¹⁰⁷ in 1886 and 1887, appears to have been the first to attempt partial and complete removal of the circumference of the cervical portion of the esophagus with the express intention of following the operation immediately with the replacement of the esophageal defect by the skin of the neck. He first experimented on dogs and performed two types of operation, either leaving posteriorly a longitudinal strip of esophageal wall from 1 to 2 cm. in width or removing the whole circumference. In the first type he reconstructed the posterior esophageal wall by lateral flaps of skin. In the second, instead of employing a vertical incision in the skin, he made two horizontal incisions distant from one another slightly more than the length of the portion of the esophagus to be resected, thus forming a bridge of skin which when undermined was freely movable. After resection, the bridge of skin was dropped back into the wound, and its upper and lower edges sutured to the posterior edges of the corresponding esophageal orifices, thus reconstructing the

106. Mikulicz, J.: Ein Fall von Resection des carcinomatösen Oesophagus mit plastischem Ersatz des excidirten Stückes, *Prag. med. Wchnschr.* **11**:93, 1886.

107. Von Hacker, Victor: Zur Pharyngo- und Oesophagoplastik, *Zentralbl. f. Chir.* **18**:121, 1891.

posterior wall of the esophagus. In both types he undertook to reconstruct the anterior wall of the esophagus by the formation of two rectangular flaps of skin, the outer edges of which he turned medially and sutured together in the median line. The skin lateral to the flaps was undermined enough to permit of its being drawn together over the inverted flaps of skin and sutured over them (Bircher²⁷ employed the same principle on a larger scale for his antethoracic skin tube).

The opportunity to carry out the operation on a human subject presently came to von Hacker.¹⁰⁷ He formed two rectangular flaps of skin before performing the resection, but as he left none of the esophageal wall behind, he brought the flaps together, sutured them in the median line and stitched their upper and lower angles to the circumference of the posterior esophageal wall. Before the second step of completing the skin tube by the formation of the anterior wall from the flaps of skin, the patient died.

In 1898, Garrè¹⁰⁸ published a report of three cases of carcinoma in the cervical portion of the esophagus, in which he performed resection. One patient lived for about a year after the operation. In another case the larynx was extirpated also and its mucous membrane used successfully for esophagoplasty, being sutured to the pharynx above and the esophagus below, thus forming a new posterior esophageal wall.

In 1908, von Hacker¹⁰⁹ reported the work done up to that time on resection of the cervical portion of the esophagus. Altogether, he reviewed twenty-five cases from the literature. In almost all of them plastic repair had been attempted, but was completed in only a few cases. The most interesting fact to be gleaned from his report is that, except for his own second case, Czerny's patient lived the longest after operation (fifteen months). That this patient thirty-one years previously had been the first to undergo resection of the cervical portion of the esophagus indicates clearly the lack of progress in this type of surgery up to this time. In 1908, von Hacker described his second case, in which, after preliminary gastrostomy, resection of nearly all the cervical portion of the esophagus was undertaken, together with the total extirpation of the larynx and the trachea down to a short distance above the jugular notch. The trachea was sutured to the skin, and the first stage of the plastic operation was done by suturing a right-sided rectangular flap of skin into the esophageal defect. Later he performed the second stage, completing the formation of the tube of skin by turning inward the two rectangular flaps of skin, joining them together in the median line

108. Garrè, C.: Ueber Oesophagus-Resection und Oesophagoplastik, Arch. f. klin. Chir. 57:719, 1898.

109. Von Hacker, Victor: Ueber Resection und Plastik am Halsabschnitt der Speiseröhre, insbesondere beim Carcinom, Arch. f. klin. Chir. 87:257, 1908.

and covering them with two lateral flaps, one longer than the other, so that the suture line was to one side and not in the median line. The third stage consisted in completing the juncture between the pharynx and skin tube. After fourteen months the patient had gained 19 Kg. (40 pounds), and on examination at the end of sixteen months after the operation was in good health.

In 1911, Lane¹¹⁰ introduced the single skin-flap method for plastic repair after resection of the cervical portion of the esophagus. He cut a horizontal flap 5 cm. deep and 12.5 cm. long with its base to the left of the neck. The flap was then reflected toward its base. The upper part of the esophagus was exposed and the carcinoma removed with a margin of uninvolved esophageal wall. The removed segment of esophagus was then replaced by folding the flap in the form of a tube in the longitudinal axis of the esophagus. The upper margin was sutured to the pharynx and the lower to the divided esophagus. After a sufficient interval for firm union of the skin esophagus to the portions of the normal esophagus at the lines of section, the attachment of the skin flap by its base to the skin of the neck was divided, and any lateral aperture which remained in the skin esophagus was closed. The danger of necrosis of the skin flap is in direct proportion to its length. The patient progressed for some time, but death occurred seven months after the operation from perforation of the carotid artery due to recurrence of the growth. Two years later, Ach¹¹¹ attempted an operation similar to that of Lane. His patient died soon afterward.

In 1913, Gluck,¹¹² commenting on the 48 per cent operative mortality among the twenty-five cases reviewed in the literature by von Hacker¹⁰⁹ in 1908, reported that he had operated in forty-seven such cases with only five deaths.

The experiments which have led to the attempted replacement of a resected portion of the esophagus by fascia had their origin in those of König,¹¹³ in 1911, who successfully reinforced esophageal suture lines by a flap of cervical fascia and platysma. Kostenko and Rubaschew¹¹⁴ went a step further and succeeded in replacing small oval resected por-

110. Lane, W. A.: Excision of a Cancerous Segment of the Oesophagus, Restoration of the Oesophagus by Means of Skin Flap, *Brit. M. J.* **1**:16, 1911.

111. Ach, A.: *Beiträge zur Oesophagus-Chirurgie*, Munich, J. F. Lehmanns, 1913, 132.

112. Gluck: Ueber Oesophago-, Pharyngo- und Laryngo-plastik, *Berl. klin. Wchnschr.* **35**:938, 1898; *Erfahrungen auf dem Gebiete der Chirurgie der oberen Luft- und Speisewege*, *ibid.* **50**:953, 1913.

113. König, Fritz: *Neue Wege der plastischen Chirurgie (Verlöthung und Ueberbrückung)*, *Arch. f. klin. Chir.* **95**:326, 1911.

114. Kostenko, M. F., and Rubaschew, S. M.: Ueber die freie Fascientransplantation, *abstr., Zentralbl. f. Chir.* **39**:1448, 1912.

tions of the cervical part of the esophagus. Razzaboni,¹¹⁵ using the peritoneum and sheath of the rectus abdominis, and Neuhoof,¹¹⁶ with autogenous fascia lata, did similar work.

Allen,¹¹⁷ in 1923, was the first to attempt the experimental replacement of the whole circumference of the resected esophagus by autogenous fascia lata. His efforts to do this in one stage were all failures because of fatal cellulitis and mediastinitis. He therefore devised a two-stage method, first placing two tubes of fascia around the esophagus, the outer tube being the longer. After several days he split the outer tube and removed the inner with the esophagus contained in it. By this method most of the animals survived, although stenosis developed in all cases. Later, Allen¹¹⁸ developed a technic for removing a portion of esophagus inside a fascial sleeve without splitting the sleeve. He placed two stout ligatures around the esophagus a short distance apart, enveloped this portion by a sleeve of fascia lata, and brought out the ends of the ligatures through the fascia. After a few days the ligatures were tied tightly, and the esophagus sloughed between them, the necrotic tissue being swallowed. In two of seven cases he failed to secure sloughing, because the ligatures were not tied tightly enough. In the remaining five cases, stenosis developed.

Neuhoof and Ziegler¹¹⁹ advocated a granulation tube method for reconstruction of the esophagus after resection. The first stage consisted of isolating the esophagus and packing it off from the surrounding structures. A week later, the packs were removed and granulation tissue had formed under them. The segment of esophagus was then excised, and a soft rubber tube securely sutured in its place. Granulations formed around the tube, which became loose and was removed. A fistula formed but finally closed completely. All the animals survived this two-stage operation, although all attempts to perform it in one stage ended in fatal cellulitis.

Schönbauer and Orator¹²⁰ performed experiments similar to those of Allen,¹²¹ using an inner and outer tube of peritoneum. One animal

115. Razzaboni, Giovanni: Ricerche sperimentali sull'autoplastica esofagea per mezzo del trapianto di lembi liberi musculo-aponeurotico-peritoneali, *Policlinico* 24: (Sect. Chir.) 417, 1917.

116. Neuhoof, Harold: Fascia Transplantation into Visceral Defects: An Experimental and Clinical Study, *Surg. Gynec. Obst.* 24:383, 1917.

117. Allen, D. S.: Experimental Reconstruction of the Esophagus with Autogenous Fascia Lata Transplants, *Ann. Surg.* 76:157, 1922.

118. Allen, D. S.: Further Experimental Reconstruction of the Esophagus with Autogenous Fascia Lata Transplants, *Arch. Surg.* 10:374 (Jan.) 1925.

119. Neuhoof, Harold, and Ziegler, J. M.: Experimental Reconstruction of the Esophagus by Granulation Tubes, *Surg. Gynec. Obst.* 34:767, 1922.

120. Schönbauer, Leopold, and Orator, Viktor: Peritoneal Transplantation zur Esophagusnaht, *Arch. f. klin. Chir.* 129:806, 1924.

121. Allen (footnotes 117 and 118).

lived for a year. The latest report in the literature on experimental surgery of the cervical portion of the esophagus is that of Carrington.¹²² After clamping the esophagus with two Kocher clamps, he placed a row of interrupted silk Lembert sutures all around and then cut through the esophagus between the clamps. The sutures were drawn tightly and the clamps released and withdrawn. The sutures were again drawn tightly as the clamps were removed, and this time were tied. Another similar layer of interrupted Lembert sutures was placed outside the first row. Each suture included muscle and adventitia. The wound in the neck was closed tightly. The experiment on only one dog was successful; fatal mediastinitis developed in all the other dogs, or, more commonly, sloughing of the esophagus that failed to hold. Carrington then changed his technic. After mobilization, the esophagus was surrounded by two narrow tapes about 5 cm. apart tied tightly enough to prevent leakage without injury of the muscular coat. An antiseptic solution, such as mercurochrome-220 soluble or a weak solution of iodine or chlorine, was introduced through a needle into the esophageal lumen between the two tapes. After time had elapsed for sterilization, the esophagus was divided and cut ends sutured together with three rows of sutures, the first continuous through all layers, the second an interrupted Lembert suture and the third consisting of six Lembert sutures which took in a long bite of tissue and were drawn only sufficiently tight to relieve the tension on the first two rows. Of eighteen such operations, he succeeded in nine; in most of the nine failures the esophagus was totally or partially divided, with resultant extensive cervical infection often associated with purulent mediastinitis. In one case only was there marked stricture, and even then the dog was kept in excellent condition. Carrington always sutured the cut ends of the esophagus with the viscus fully expanded, and it was on this part of his technic that he explained the absence of stricture in his results.

*Thoracic and Cardiac Portions (End-to-End Anastomosis).—*Although the cardiac portion of the esophagus is intraperitoneal, the operations on it and on the intrathoracic portion are so intimately connected that the operative procedures on these two parts of the esophagus will be considered simultaneously.

Resection of the thoracic and cardiac portions of the esophagus followed by end-to-end anastomosis has not yet passed beyond the experimental stage, as the clinical indications for its performance are not likely to be encountered frequently.

122. Carrington, G. L.: Experimental Surgery of the Esophagus: Some Factors and End Results, *Ann. Surg.* 86:505, 1927.

In 1901, Dobromysslów¹²³ reported the first successful intrathoracic suture of a resected esophagus. He made a large skin flap with its base posteriorly, extending from the sixth to the tenth rib vertically; it was about from 10 to 15 cm. in length. Resection of the ribs probably followed, although this was not mentioned. After incising the parietal pleura and laying bare the lower part of the esophagus, he divided the vagi and resected from 3 to 4 cm. He united the ends by two rows of silk sutures. Before the thoracic flap was sutured in place, the air was sucked out of the pleural cavity by negative pressure. Three weeks later, complete union of the suture line was found to have taken place, with slight proximal dilatation of the esophagus.

In spite of this apparent mastery of intrathoracic esophageal surgery, subsequent work in the same direction has not fulfilled the promise of success which Dobromysslów's performance seemed to give, even though shortly afterward the differential pressure chamber invented by Sauerbruch and the positive pressure apparatus of Brauer came into use and by their prevention of collapse of the lung during operation and pneumothorax afterward gave a great impetus to intrathoracic surgery.

In 1905, Sauerbruch¹²⁴ published two articles dealing with his experimental intrathoracic work on dogs. He introduced the intercostal incision in place of the more tedious and mutilating flap and resection method. Opening a pleural cavity through an intercostal incision is so simple and gives such excellent exposure of the thoracic part of the esophagus that it has been universally adopted in experimental work. Sauerbruch first of all tried end-to-end suture of the esophagus after resection and met with little success as his sutures continued to tear out.

In 1913, Omi and Karasawa¹²⁵ obtained some surprisingly good results in experimental operations on the thoracic portion of the esophagus. They used silk sutures in three layers, the first through the mucosa, the second through the muscle and adventitia and the third a continuous external Lembert suture. Of nine divisions of the esophagus with end-to-end anastomosis, seven were successful. In consequence of their results, they felt that a carefully made suture of the esophagus is sufficiently reliable to warrant its adoption in operations on human beings.

123. Dobromysslów, W. D.: Ein Fall von transpleuraler Oesophagotomie im Brustabschnitte, abstr., *Zentralbl. f. Chir.* 28:18, 1901.

124. Sauerbruch, F.: Die Chirurgie des Brustteils der Speiseröhre: Eine experimentelle Studie, *Beitr. z. klin. Chir.* 46:405, 1905; Die Anastomose zwischen Magen und Speiseröhre und die Resektion des Brustabschnittes der Speiseröhre, *Zentralbl. f. Chir.* 32:81, 1905.

125. Omi, K., and Karasawa, Z.: Beitrag zur Chirurgie der Speiseröhre, *Deutsche Ztschr. f. Chir.* 124:574, 1913.

Thoracic and Cardiac Portions (Esophagogastrostomy).—Esophagogastrostomy as a method of restoring the continuity of the alimentary tract after resection of the thoracic portion of the esophagus has proved more popular than any other operation for this purpose.

Biondie,²¹ in 1895, was the first to carry out this procedure, performing it on dogs. To him also goes the credit of being the first to expose the esophagus by the transthoracic route. He employed a paravertebral incision followed by the resection of two or three ribs and incision of the parietal pleura. The stomach was pulled up through the diaphragm, the lower end of the esophagus cut through and the oral end sutured into the fundus of the stomach, which was then replaced in the abdomen. Biondie stated that the technic was difficult, particularly on account of the movement of the diaphragm, and pointed out that in the human subject the amount of esophagus to be resected for carcinoma might be so great that replacement of the stomach in the peritoneal cavity after the esophagogastrostomy might not be possible.

In 1904, Mikulicz¹²⁶ gave an account of his researches in intrathoracic surgery carried out in the Sauerbruch differential pressure chamber. He pointed out that it is difficult enough to reunite a transected esophagus because of tension, but much more difficult to reunite one in which a portion has been resected. Therefore he let alone the direct juncture of the two ends after resection and devised two other methods of dealing with the problem, the choice of method depending on whether the portion to be resected was at the lower end or higher up in the thorax. In the first case, after opening the pleural cavity, he pulled up the stomach and anastomosed it to the oral end of the resected segment of the esophagus. He found that in dogs and cadavers a good part of the cardiac end of the stomach could be drawn up into the pleural cavity. The wall of the stomach was stitched to the margin of the diaphragmatic opening, and the esophagogastric juncture remained within the pleural cavity. One dog in which this operation was performed had, at the time of writing, lived six weeks without any disturbance of digestion or nutrition. Another animal, in which 2.5 cm. of the lower end of the esophagus had been removed and esophagogastrostomy performed in this way, lived four weeks, and at necropsy the suture line was found to be intact and moderately stenosed. Disease of the lungs or pleura was not present. Mikulicz suggested that the displaced stomach might be replaced in the abdomen and the diaphragm sutured to the esophageal wall above the esophagogastric juncture which would thus become intraperitoneal. He performed this operation several times.

128. Voelcker: Ueber Exstirpation der Cardia wegen Carcinoms, *Verhandl. d. Verhandl. d. deutsch. Gesellsch. f. Chir.* 27:252, 1898.

In 1905, Sauerbruch,¹²⁴ because he considered tension the main cause of failure in his work on end-to-end anastomosis of the esophagus after resection, brought up the stomach into the pleural cavity and anastomosed the oral end of the resected segment of the esophagus to it both by end-to-end anastomosis and by implanting the esophagus into the stomach like the tube in a Witzel gastrostomy. In most of his experiments the sutures tore out. These failures led him to adopt the button for intestinal anastomosis. This proved so successful that he abandoned the use of sutures altogether. He stated that he had operated on eleven dogs without a death, although more than 7 cm. of the esophagus was resected. He also introduced a two-stage operation for the removal of the cardiac portion of the esophagus. The first stage consisted of thoracotomy with transection of the lower part of the esophagus and inversion of the lower end into the stomach followed by esophagogastrostomy. The second stage was undertaken after fourteen days, at which time laparotomy was performed, the stomach opened and the intragastric esophageal projection cut off; the stomach and laparotomy wound were closed. He performed this operation on cadavers and believed it to be feasible on the living subject. He mentioned clinical experience in three cases in which thoracotomy had been performed with a view to resection of esophageal carcinoma. All three tumors proved to be inoperable, and all the patients died.

In 1907, Wendel¹²⁷ operated on a patient who had carcinoma of the cardia and lower end of the esophagus; he used the transpleural route, bringing up the stomach through the diaphragm. After resection of the growth, he closed both the esophagus and the stomach and performed lateral esophagogastrostomy by means of a button. The patient died the next day of hemorrhage. This is the first case reported in which this operation was performed on a living subject.

In 1908, Voelcker¹²⁸ reported the first successful case of extirpation of a carcinoma of the cardia following two failures. After laparotomy through an incision parallel to the left costal margin, he cut the cardia below the tumor, freed the esophagus at its hiatus and pulled down about 4 cm. Then the esophagus was cut through above the tumor, and its oral end anastomosed to the stomach near its greater curvature. Gastrostomy was performed near the pyloric end. After four weeks of feeding through the fistula, nutrition by mouth was begun. In another month the fistula closed, and the patient ate normally. Data concerning this case have not appeared in the literature subsequently.

127. Wendel, W.: Beitrag zur endothorakalen Oesophaguschirurgie, Arch. f. klin. Chir. **83**:635, 1907.

128. Voelcker: Ueber Exstirpation der Cardia wegen Carcinoms, Verhandl. d. deutsch. Gesellsch. f. Chir. **37**:126, 1908.

In 1909, Meyer¹²⁹ emphasized the importance of avoiding contamination of the mediastinum and pleura with the highly infectious esophageal mucous secretion, and devised a method of esophagogastrostomy whereby he sought to achieve this end. The essential points were: (1) drawing up the stomach into the pleural cavity and suturing the diaphragmatic peritoneum to the wall of the stomach; (2) division of the esophagus below the supposed tumor between a clamp below and a ligature above followed by inversion of the distal stump; (3) division of the esophagus above the supposed tumor between the clamp below and a ligature of absorbable catgut above; (4) incision of the stomach through serosa and muscularis and suture of the upper edge to the posterior wall of the esophagus with two layers; (5) opening of mucous membrane of the stomach and introduction of the ligated oral end of the esophagus, and (6) completion of the esophagogastric juncture by two layers of sutures between the lower edge of the incision in the stomach and the anterior wall of the esophagus. In six dogs operated on by this method, two functioning anastomoses were obtained. Meyer suggested: 1. Stricture may be avoided by dividing the esophagus with scissors instead of cautery, as burns show a greater tendency to contract than cuts, and that the esophagus should be divided obliquely instead of at right angles to its longitudinal axis if length permits. 2. Contraction of the gastric wound around the esophagus can be averted by elliptical excision of the serosa followed by a linear incision of the mucosa.

In 1909, Janeway and Green¹³⁰ operated on a large series of dogs, performing intrathoracic esophagogastrostomy alone; after resection of the lower part of the esophagus they used a specially designed button and reinforced the anastomosis thus made by suture. In sixty-nine operations, they successfully accomplished resection of the cardia and lower thoracic portion of the esophagus in four cases and lateral anastomosis without resection in six. They stated that their work demonstrated that speed, absolute asepsis and scrupulous care in the minimizing of trauma are essentials of success in esophageal operations. For these reasons, they adopted the button instead of sutures for anastomosis.

129. Meyer, Willy: *Oesophagogastrostomy After Intrathoracic Resection of the Oesophagus*, *Ann. Surg.* **50**:175, 1909; *Cancer of the Esophagus from the Standpoint of Intrathoracic Surgery: A Report of Four Resections*, *Surg. Gynec. Obst.* **15**:639, 1912.

130. Janeway, H. H., and Green, N. W.: *Experimental Intrathoracic Esophageal Surgery*, *J. A. M. A.* **53**:1975 (Dec. 11) 1909.

In 1909, Tiegel¹³¹ also used a modification of the button for intestinal anastomosis with some success, employing surgical procedures similar to those of Janeway and Green. He performed this type of operation once on man. The patient died eleven hours afterward.

In 1918, Bircher¹³² resected two carcinomas which involved the lower end of the esophagus and the cardiac part of the stomach. His technic was similar to that of Voelcker,¹²⁸ in 1908; he used the abdominal route and avoided opening the pleural cavity. In the first case, the esophagus was freed at its hiatus and easily drawn down above the upper limits of the tumor. This was then removed, the esophagus closed by ligature and the wound in the stomach closed, except for about 3 cm. near the greater curvature. Five long sutures were introduced into the wall of the esophagus, and an incision 2 cm. long was made on the anterior wall of the stomach about 5 cm. below the upper opening. Forceps were introduced through the lower opening in the stomach, passed through the upper opening and the long esophageal sutures seized. The esophagus was brought within the stomach through the upper opening by traction and made fast to the stomach after the manner of a Senn gastrostomy, three rows of sutures being used. A fourth row of sutures attached the stomach to the diaphragm all around the esophagus, thus completely covering it with peritoneum. The long esophageal sutures were cut, and the lower part of the opening in the stomach was used for a Kader type of gastrostomy. The patient, a woman, aged 63, was able to eat any kind of food one month after operation and survived for eighteen months. In the second case, Bircher used almost the same technic, except that he implanted the esophagus into the stomach after the manner of Witzel's gastrostomy. The patient died of cardiac insufficiency three days after the operation. At necropsy, the stomach was found adherent to the diaphragm. Bircher said that for primary union, operation should take place through the abdomen, and an attempt should be made to avoid the thorax entirely. Whereas Voelcker was satisfied with two layers of sutures for the implantation of the esophagus, Bircher used three, so that the esophagus was covered with peritoneum as much as possible.

In 1919, Bengolea¹³³ removed a carcinoma of the thoracic portion of the esophagus in a woman, aged 37, by the transpleural route, using a

131. Tiegel, Max: *Zur Chirurgie des Oesophagus*, Beitr. z. klin. Chir. 65:314, 1909; *Die chirurgische Behandlung des Speiseröhrenkrebses ihr gegenwärtiger Stand und ihre Aussichten für die Zukunft*, München. med. Wchnschr. 57:896, 1910.

132. Bircher, Eugen: *Operative Heilung eines Karzinomes, am Uebergang des Oesophagus in die Kardia*, Cor.-Bl. f. schweiz. Aerzte. 48:467, 1918.

133. Bengolea, A. J.: *Radical Resection of the Oesophagus for Carcinoma*, Surg. Gynec. Obst. 29:413, 1919.

Torek incision. The stomach was brought up through the diaphragm and esophagogastrostomy performed with the aid of a wooden bobbin placed in the oral end of the esophagus, which was invaginated into an opening on the fundus of the stomach. Closed drainage was used in accordance with Kenyon's technic. This proved inefficient, and, the wound had to be reopened, when serosanguineous fluid, which later became purulent, was evacuated. The patient died thirty-seven days after the operation.

In 1920, Kirschner⁶² used an abdominothoracic route to operate in two cases of carcinoma of the lower end of the esophagus also involving the cardiac part of the stomach. The incision began about midway between the xiphoid process and umbilicus, extended laterally to the left costal margin and from there along the seventh intercostal space. After dividing the diaphragm down to the esophageal hiatus, he freed and removed the tumor. He then mobilized the stomach according to his method, which has been described. The oral part of the esophagus was extracted through the neck, after the manner of Ach,¹¹¹ and brought downward under the skin of the chest. The mobilized stomach was then brought up onto the anterior thoracic wall subcutaneously, with the ultimate aim of joining the esophageal and gastric orifices by skin esophagoplasty, thus making a new artificial esophagus. The first patient died the day following operation, and the second survived five days. In the second case, the lower 3 cm. of the subcutaneous oral end of the esophagus necrosed, but the stomach was in good condition. Mediastinitis was present.

In 1922, Kümmell, Jr.,¹³⁴ introduced a new method for the operative treatment of carcinoma of the thoracic or cardiac portion of the esophagus. After freeing the esophagus in the neck and at the diaphragmatic hiatus, he mobilized the stomach after the manner of Kirschner. One index finger was inserted downward into the cervical wound along the esophagus and the other upward through the hiatus. Working with these fingers, he separated the esophageal wall from its surrounding mediastinal tissue until the two index fingers came in contact with one another, the esophagus being thus loosened in its bed. It was pulled upward until the cardia appeared in the cervical wound, so that the stomach now filled the mediastinum. The tumor was resected and esophagogastrostomy performed, the line of suture being extrathoracic and not to be replaced in the wound until it was known to hold. In this way Kümmell completed the immediate formation of a new esophagus in one stage; he believed that the stomach acts as a good tampon to stop bleeding from the esophageal bed. In spite of the fact that the

134. Kümmell, Hermann, Jr.: Operation des Oesophaguskarzinoms, *Deutsche med. Wchnschr.* **36**:1886, 1910; Ueber intrathorakale Oesophagusplastik, *Beitr. z. klin. Chir.* **126**:264, 1922.

five dogs and two patients operated on in this way died of rupture of the pleura with hemothorax within twenty-four hours of the operation, Kümmell was enthusiastic, and said that the advantages of his method lay in the avoidance of the larger mutilating operations; the extra-thoracic opening and juncture of the stomach and the esophagus, with prevention of the dreaded lethal mediastinitis due to suture or button insufficiency; the relatively rapid completion in one stage, and the immediate formation of a useful esophagus. In his experiments on animals and in clinical cases, he did not notice a disturbance in the nutrition of the wall of the mobilized and displaced stomach.

In 1923, Miller and Andrus⁵⁴ performed intrathoracic esophago-gastrostomy experimentally on dogs. They used the bulkhead suture of Halsted for the anastomosis. After the lower part of the esophagus had been resected and the cardiac stump inverted, the site on the stomach for the implantation of the esophagus was selected, and a circular area, about twice the size of the esophageal lumen, was outlined by an incision which passed through the serous and muscular coats. A temporary occluding ligature was obtained by threading a needle with strong silk and grasping the tissue in the bed of this incision at close intervals. The lumen of the esophagus was closed in a similar fashion at the upper limit of the proposed resection. Both the stomach and the esophagus were cut away just distal to the occluding ligatures; the resultant stumps were cauterized with cautery and phenol and brought into apposition by mattress sutures of fine silk. Just before the last two or three of these sutures were tied, the loop of each occluding ligature was drawn into plain view and cut and these threads pulled out; the lumen was thus reestablished. Care was taken to grasp the submucosa with the first sutures; then followed a row of sutures which grasped the muscular coats of the stomach and esophagus. The operation was performed eighteen times. Four dogs died within a few hours from shock and hemorrhage, and three other operations failed, two because of tension and one because of the occurrence of gangrene in the part of the gastric wall involved in the suture. All of the remaining eleven dogs showed an intact suture line and functioning anastomosis, despite the occurrence of death from infection, dilatation of the stomach and diaphragmatic hernia. Reference has been made to the work of these authors on the structure of the esophagus of human beings and the mobilization of the stomach. They concluded that resection and suture in situ of the esophagus were not beyond the bounds of possibility but rather offered definite grounds for hope.

In dealing with the resection of the lower part of the esophagus with subsequent esophagogastronomy, Heuer, Andrus and Bell,¹³⁵ in 1925,

135. Heuer, G. J.; Andrus, W. D. W., and Bell, H. G.: The Experimental Transplantation of the Diaphragm as an Adjunct in the Treatment of Lesions of the Lower End of the Oesophagus, *Ann. Surg.* 81:273, 1925.

sought to convert the procedure into an abdominal operation by the upward transplantation of the diaphragm, hoping in this way to avoid the well recognized danger of intraplanation of the diaphragm and to test the feasibility of the procedure, and later to perform intra-abdominal esophagogastrostomy after resection of the esophagus. In the first series of dogs, the thorax was entered on the left side, and the periphery of the diaphragm was detached from its costal attachment and sutured to the parietal pleura at a higher level. In the second series, these authors not only transplanted the left half of the diaphragm, but also divided it down to the esophageal hiatus, freed the lower part of the thoracic esophagus, and sutured the diaphragm to its wall at a higher level. In a third series, freeing the esophagus only at its hiatus accompanied the upward transplantation of the diaphragm. In the first series, good results were obtained. In the second, there was a mortality of about 30 per cent, the result of infection; postoperative vomiting was common, apparently due to constriction of the esophagus at its new hiatus. One case of diaphragmatic hernia occurred in this series. Two dogs comprised the third series; both recovered promptly from the operation without vomiting and were killed later. Diaphragmatic hernia was found in one case.

In six animals of the second and third series, intra-abdominal esophagogastrostomy was performed after resection of the lower part of the esophagus. The Halsted bulkhead type of suture was used as in the intrathoracic work of Miller and Andrus. An intercostal incision was made into the abdomen, and comment was made on the good exposure obtained and the fact that the operation was not difficult. The authors submitted a patient suffering from carcinoma of the lower end of the esophagus to this two-stage procedure. Although the history was only of two months' duration, the tumor was 7.5 cm. long and 5.5 cm. in diameter. Besides upward displacement of the diaphragm, the tumor was freed and the diaphragm sutured to the esophageal wall above it. The second stage was not undertaken, as the patient died forty-eight hours after the first operation. At necropsy, gangrene was found involving the proximal half of the growth and extending upward on the uninvolved esophagus to a point about 1 cm. above the new hiatus. At one point on the right anterolateral wall, perforation had occurred in the gangrenous area allowing leakage into the pleural and abdominal cavities. They concluded that it would be better to leave the freeing of the esophagus from its bed until the second stage.

In 1926, Fischer¹³⁶ introduced still another technic for the safe anastomosis of the esophagus and stomach intrathoracically. After

136. Fischer, Herman: Esophageal Implantation into Stomach After Intrathoracic Resection of the Esophagus for Carcinoma: A New Method, *Arch. Surg.* 12:241 (Jan.) 1926.

opening the pleural cavity by Sauerbruch or Torek's incision, he performed left phrenicotomy; this operation, by abolishing the respiratory movements of the side of the diaphragm, relaxes that structure, making easier the subsequent fixation of the stomach to its cut edge and ensuring undisturbed healing of the anastomosis. To effect this, he cut a sero-muscular quadrilateral flap from the upper part of the stomach with its base downward, and to the denuded submucosa he sutured the sides of the oral end of the esophagus, only its distal part entering the lumen of the stomach through a small incision in the submucosa, near the base of the flap. The flap was then sutured over the esophagus and broad Lembert sutures covering the flap finished the anastomosis. The suture which occludes the oral end of the esophagus is of plain catgut, which will be digested by the gastric juices in a few hours, and thus the esophageal lumen will be rendered patent. From experimental work done on the cadaver, Fischer has satisfied himself that his technic is feasible and not difficult.

In 1927, Gohrbandt¹³⁷ described an operation for carcinoma of the lower end of the esophagus somewhat similar to that of Kümmell¹³⁴ in that the mobilization of the viscus was carried out in the same way, namely, by the insertion of one forefinger down from the wound in the neck, and the other up through the diaphragmatic hiatus and by a circular and progressive motion eventually bringing about the meeting of the fingers near the level of the hilum. The esophagus was then pulled down and the tumor resected in the peritoneal cavity. A Babcock probe was then introduced through the neck along the side of the esophagus into the abdomen and firmly sutured to the distal part of the oral end. The probe was drawn up out of the wound in the neck, bringing the esophagus along with it. The esophagus was then transposed under the skin of the anterior thoracic wall. A portion of the stomach was drawn up under the skin for later plastic anastomosis with the ante-thoracic esophageal stump. The patient was to be nourished through a Witzel gastrostomy until the anastomosis was completed.

Gohrbandt reported six cases. In the first case, a carcinoma situated just above the cardia was resected intra-abdominally and esophagogastrostomy performed; the patient lived for six months after the operation and died of an intercurrent disease. By the tunneling method described, the author attempted the removal of five carcinomas. Of these, two proved to be inoperable; one patient died of pneumonia three days after the operation; in another the tumor perforated while being loosened, with a fatal result, and in a third case, death occurred on the ninth day following operation from a phlegmon of the ante-thoracic site of anastomosis of the stomach and esophagus.

137. Gohrbandt: Zur Operation des intrathorakalen Oesophaguskarzinoms, Zentralbl. f. Chir. 54:26, 1927.

Thoracic and Cardiac Portions (Transposition of the Oral End).—

In 1898, Levy¹³⁸ devised an ingenious, although rather impracticable, method of removing the thoracic part of the esophagus in dogs. He first performed gastrostomy and afterward severed the esophagus in the neck, suturing the oral end to the skin. He next brought a thread that had been introduced into the aboral end of the divided esophagus through a stomach tube out of the gastrostomy opening. He closed the upper end of the lower part of the esophagus in the neck by tying it with the thread. By pulling slowly on the thread, he inverted the esophagus and gradually pulled it out through the gastrostomy opening. When the cardiac part appeared, he ligated and cut the stump, sliding it back into the stomach. One of the animals lived six weeks. Levy tried this method on the cadaver, but he did not succeed in pulling out all the esophagus as he had done in dogs, as the outer longitudinal muscle fibers separated and remained behind. Consequently, he concluded that the procedure was not possible in man.

Mikulicz,¹³⁹ in 1904, was the first to introduce antethoracic subcutaneous transposition of the oral end of the esophagus after resection of its upper thoracic part. After intrathoracic resection, both ends were inverted and the thorax closed. The oral end of the esophagus was then brought out through an incision at the anterior border of the left sternomastoid muscle. Mikulicz said that because of the loose attachment of the esophagus in the mediastinum he succeeded without difficulty. Then the bared esophageal stump was brought under the skin in front of the pectoralis major and its end fixed to the edges of a small transverse incision over the second intercostal space. The wound in the neck was closed tightly. It was later proposed to make a plastic juncture between the esophagostomy and a gastrostomy opening which, of course, had to be performed to provide the animal with nourishment temporarily.

In 1904, Kelling¹⁴⁰ also introduced a method of transposition of the oral end of a transected esophagus. He believed that the opening of the esophagus within the thorax was the chief factor of the high mortality consequent on intrapleural esophageal operations, since infection of the pleura or mediastinum was almost certain to occur. Therefore, he sought to operate aseptically in the pleural cavity and mediastinum by refraining from opening the esophagus here. He

138. Levy, William: Versuche über die Resection der Speiseröhre, Arch. f. klin. Chir. **56**:839, 1898.

139. Mikulicz, von: Chirurgische Erfahrungen über die Sauerbruch'sche Kammer bei Unter- und Ueberdruck, Verhandl. d. deutsch. Gesellsch. f. Chir. **33**: 34, 1904.

140. Kelling, Georg: Zur Frage der intrathorakalen Operation der Speiseröhre, Zentralbl. f. Chir. **31**:609, 1904.

performed an intrathoracic operation and loosened the tumor from its surrounding tissues, closing the thorax immediately afterward. The abdomen was then opened and the esophagus freed from the diaphragm. The cardiac portion of the esophagus was divided and the distal end closed; in the oral end he placed a wooden cylinder, and after tying the esophagus around this, he enclosed the end in a rubber membrane. He now pulled on a thread which had previously been passed down the esophagus and fastened to the wooden cylinder. The latter was pulled up, drawing with it the esophagus which was pulled out through an incision in the neck and after resection of the tumor drawn through a tunnel under the skin of the chest, being sutured to the edges of a transverse incision in the skin. He performed a skin esophagoplasty between the esophagostomy and the gastrostomy openings, with poor results.

In 1910, Wendel¹⁴¹ performed operations in two cases of thoracic esophageal carcinoma, in each case bringing one end of the resected esophagus into the thoracotomy wound with a view to a future plastic operation. In the first case, the carcinoma was at the height of the bifurcation of the trachea; after the esophagus had been cut through below the tumor, the aboral end was brought forward into the thoracotomy wound in the anterior axillary line and sutured in position. The oral end of the esophagus was brought upward through an incision in the neck after the preliminary freeing from its surrounding tissues, and the tumor was then resected extrapleurally. The esophagus was then stitched into the wound in the neck. Death occurred from bilateral pneumothorax nine hours after the operation. In the second case, the carcinoma was in the lowest part of the thoracic portion of the esophagus. After the esophagus was cut through above the tumor, the aboral end was closed and the oral end was brought forward and sutured into the thoracotomy wound. Through a laparotomy incision, the tumor was pulled down and extirpated together with part of the cardiac end of the stomach. The wound in the stomach was reduced in size to that of a gastrostomy opening and sutured into the abdominal wall. The patient survived the operation only twenty-four hours. Collapse of the left lung was found at necropsy.

In 1913, Ach¹⁴¹ and Zaaier¹⁴² succeeded in removing a carcinoma of the cardiac portion of the stomach and esophagus. Torek⁹⁷ removed a carcinoma from the thoracic portion of the esophagus. Ach planned his operation so that the pleural cavity should not be opened, working

141. Wendel, W.: Zur Chirurgie des Oesophagus, *Arch. f. klin. Chir.* **93**:311, 1910.

142. Zaaier, J. H.: Erfolgreiche transpleurale Resektion eines Cardiacarcinoms, *Beitr. z. klin. Chir.* **83**:419, 1913.

only in the neck and abdomen; he decided to remove the upper portion of the esophagus by invagination. He performed the operation first on dogs and then on four patients. A long laparotomy incision was made parallel to the left costal margin. The cervical portion of the esophagus was then exposed and mobilized by blunt dissection. The costal margin was retracted well upward so that good exposure was obtained. The diaphragm around the esophageal hiatus was freed and the tumor pulled down, both vagi being cut. The esophagus was clamped above the tumor, and a ligature about 1 meter long was tied around the esophagus above the clamp. A second clamp was applied above the tumor and the esophagus divided between them. A long flexible steel rod with an eye in its end was passed down the esophagus until it came in contact with the ligated oral end. A suture was passed through the esophageal wall, and the eye of the rod and was left about 12 cm. long. The rod was carefully withdrawn; the suture, as it was pulled taut, inverted the walls of the esophagus. The whole esophageal tube was thus extracted until the lower invaginated end appeared in the cervical wound, when the extraction ceased. The long ligature was secured from the invaginated funnel and fixation suture through the eye of the sound cut by the anesthetist. By pulling on the ligature, the invaginated esophagus was evaginated through the cervical wound and drawn through a tunnel under the skin of the sternum to a small transverse incision through which it was brought onto the surface of the chest. The tumor was then resected, the wound in the stomach closed and gastrostomy performed. Ach reported three cases in which he had performed operations by this method. In his second and third cases, instead of performing gastrostomy, he brought up the distal part of the stomach remaining after resection on to the anterior thoracic wall and placed it subcutaneously, thus performing an inferior esophagoplasty. All three patients died within fourteen days. He also reported fifty-five operations on dogs, most of which were intrathoracic resections, with success in only three.

Later, Ach¹⁴³ reported a fourth case of carcinoma of the cardiac portions of the esophagus and stomach in which operation was performed by his combined cervical and abdominal technic. He succeeded in removing the tumor, but the patient died seventeen days after the operation from "insufficiency of the gastric fistula."

Zaaijer¹⁴⁴ followed a plan similar to that which had been used in 1911 in his case of "oesophagostomia thoracalis" and performed the

143. Ach, A.: Beitrag zur Oesophaguschirurgie, München. med. Wchnschr. 60:1115, 1913.

144. Zaaijer, J. H.: Ueberdrücknarkose und experimentelle Ösophagus-resektion, Zentrabl. f. Chir. 38:992, 1911; Oesophagostomia thoracalis, Beitr. z. klin. Chir. 77:497, 1912.

operation in two stages. The first consisted of extensive subperiosteal resection of the lower six ribs on the left side, from the angle forward for about 10 cm. This caused sinking in of the wall of the chest, thereby rendering the esophagus and cardia much nearer the surface of the chest. After the patient had recovered from this operation, the second stage was undertaken. A long curved incision was employed, beginning in the hypochondrium below and extending upward and backward in the posterior axillary line as far as the lower angle of the scapula, and in this way laparothoracotomy was performed. The diaphragm was cut through down to the esophageal hiatus and there freed. The lower part of the esophagus was mobilized and brought, with the stomach, into the wound. Zaaier next cut through the stomach below the tumor, closed it and returned it to the abdomen, and then sutured the diaphragm. The esophagus with the tumor at its lower end was brought out through the wound, and the parietal pleura was sutured to the wall of the esophagus about 4 cm. above the upper margin of the tumor. Then followed closure of the pleural and peritoneal cavities. The tumor was removed by cutting through the healthy esophagus above it with thermocautery after a few days. The distance between the thoracic esophagostomy opening and the gastrostomy opening was provisionally overcome by an apparatus so constructed that food could be taken by mouth. The patient left the hospital fourteen days after the second operation.

Torek,⁹⁷ too, preferred to perform extrapleural resection of the esophageal carcinoma in his case, in order to do away with leakage from the oral end after resection. He also decided to pay particular attention to the avoidance of rough handling of the vagi. The patient was a woman, aged 67, with a carcinoma of the thoracic portion of the esophagus just below the lower border of the transverse arch of the aorta. The thoracic incision ran the whole length of the seventh interspace and extended upward posteriorly; the seventh, sixth, fifth and fourth ribs were divided near their tubercles. On retraction good exposure was obtained. The tumor was fairly fixed, and there was some difficulty in separating it from the arch of the aorta and the left bronchus, the latter sustaining a longitudinal cut during the dissection requiring repair by silk suture, which acted satisfactorily. Torek then dissected the esophagus free from its attachments all the way up to the neck, divided it with cautery a safe distance below the carcinoma after double ligation, and brought out the oral end with its tumor through an incision in the neck at the anterior border of the left sternomastoid. Thus the danger of infection of the mediastinum and pleural cavity from leakage of the oral end of the esophagus was obviated. The remaining lower end was crushed, ligated and invaginated, and the thorax closed without drainage. The portion of the esophagus which

was hanging out of the neck was drawn through a tunnel under the skin between the wound in the neck and a transverse incision over the second intercostal space; it was then brought to the surface through this incision, the carcinoma cut off, and the fresh rim of the esophagus sutured to the edges of the transverse incision. The wound in the neck was then closed. The patient made a good recovery and was nourished through the gastrostomy tube until the eighth day, after which time the outer end of this tube was introduced into the esophagostomy opening for the purpose of allowing the patient to carry out mastication and deglutition in the normal manner. Soon afterward she was able to take all varieties of food which could be chewed into an almost fluid state. In 1925, Torek¹⁴⁵ published a follow-up report on this case, telling of the patient's happy state and freedom from recurrence, and a year later stated¹⁴⁶ that she had died of pneumonia at the age of 79, after having been in good health up to three days before death. The patient had lived more than twelve years after the operation. Torek's case thus takes its stand as being the most outstanding and impressive in thoracic esophageal surgery. It is the only case in which the results obtained through surgical procedures have definitely exceeded those obtained by palliative measures and those obtained in many cases of carcinoma of more accessible organs when treated surgically. Although it is well known that for one patient, for example, with gastric or mammary carcinoma who survives operation for as long as twelve years, there are many who, although less fortunate, will live for three, four or five years; never before or since Torek's operation have there been any such promising results from the surgical treatment of esophageal carcinoma.

Unger¹⁴⁷ performed the same operation as did Torek, and his patient died five days afterward.

In 1914, Baumgartner¹⁴⁸ operated on a man with carcinoma of the thoracic portion of the esophagus. The patient died six hours after the completion of the operation. Baumgartner employed a technic similar to that of Torek but with minor differences. He chose to operate on the right side, mainly because of the absence of the aorta

145. Torek, F.: Carcinoma of the Thoracic Portion of the Esophagus: Report of a Case in which Operation was Done Eleven Years Ago, *Arch. Surg.* **10**:353 (Jan.) 1925.

146. Torek, F.: Surgical Treatment of Carcinoma of Esophagus, *Arch. Surg.* **12**:232 (Jan.) 1926.

147. Unger, Ernst: Zur Chirurgie des Oesophagus im Thorax, *Berl. klin. Wchnschr.* **50**:2090, 1913; Zur Chirurgie des intrathorakalen Oesophaguscarcinoms, *Arch. f. klin. Chir.* **106**:31, 1915.

148. Baumgartner, Amédée: Extirpation de l'oesophage thoracique pour cancer à l'aide de la respiration artificielle, *Presse méd.* **1**:34, 1914.

and the ease with which the azygos vein can be dealt with. He not only cut ribs near their tubercles, but resected one of them to obtain better exposure. He finally resected the tumor intrathoracically before transposing the oral end of the esophagus subcutaneously. Necropsy showed that the right pleural cavity contained about 0.75 liter of bloody fluid; a vessel which could be said definitely to be the source of the hemorrhage was not found.

In 1915, Meyer¹⁴⁹ reported on further experience with resection of the thoracic portion of the esophagus for carcinoma in four cases. All of the patients died. In three cases, he planned to restore the continuity of the esophagus with the aid of an extrathoracic Beck-Jianu tube. In the other case, he performed the Torek operation. Meyer, commenting on drainage of the pleural cavity after operations on the esophagus, said that his experience had convinced him that when Torek closed the thoracic cavity without drainage he was favored with remarkable luck. Meyer believed that it is the surgeon's duty to drain the thorax immediately after the operation in all cases of resection of the esophagus for carcinoma.

In 1922, Hedblom¹⁵⁰ resected a carcinoma involving the lower end of the esophagus and cardiac part of the stomach. He employed Zaaier's method with the modification of performing the thoracoplasty in three stages instead of in one stage as Zaaier had done, resecting the fifth to the eleventh ribs from their angles to the costal cartilages. His incision for resection extended from a point to the left of the median line below the costal margin upward and backward to the level of the fourth rib in the midaxillary line. Through this he opened both peritoneal and pleural cavities, split the diaphragm down to the hiatus and, after mobilizing the lower end of the esophagus, removed its lower 4 cm. together with the cardiac part of the stomach. The stomach was sutured to the lower part of the wound below the diaphragm and the esophagus to the wound above that structure. A month after the resection the patient had gained several pounds and was taking soft food by mouth, the esophageal and gastric stomas being connected by tube.

In 1922, Levy¹⁵¹ reported a series of operations performed on dogs in 1913 and 1914. He began to resect the cardiac portions of the

149. Meyer, Willy: Further Experience with Resection of Oesophagus for Carcinoma, *Surg. Gynec. Obst.* **20**:162, 1915; Extrathoracic and Intrathoracic Esophagoplasty in Connection with Resection of the Thoracic Portion of the Esophagus for Carcinoma, *J. A. M. A.* **62**:100 (Jan. 10) 1914.

150. Hedblom, C. A.: Combined Transpleural and Transperitoneal Resection of the Thoracic Oesophagus and the Cardia for Carcinoma, *Surg. Gynec. Obst.* **35**: 284, 1922.

151. Levy, William: Weitere Beiträge zur Resektion der Speiseröhre, *Arch. f. klin. Chir.* **119**:20, 1922.

esophagus and stomach by a two-stage operation, the first being extensive thoracoplasty for the purpose of collapsing the wall of the chest and thus bringing the esophagus nearer to the surface of the chest and facilitating its exposure. He treated the resected portion of the stomach and esophagus in the same manner as Zaaizer had done. In ten operations there were six successes; the four failures were due to empyema. He pointed out that in this operation the stomach can be brought up to any level required by the esophagus, as the diaphragm can be sutured to the wall of the chest at any desired height. Levy made a small plastic skin tube to connect the esophageal and gastric orifices.

In 1924, Lotheissen¹⁵² reported ten cases of carcinoma of the thoracic portion of the esophagus in which Torek's methods of operating were used. With the exception of two patients whose lesions were inoperable and who lived one and three months respectively after operation, all died within a few hours. Necropsy showed variously mediastinitis, empyema or collapse of the lung.

In 1925, Eggers⁹⁸ successfully removed a carcinoma of the thoracic portion of the esophagus by Torek's technic. Both vagi were sharply divided without disturbing the patient's condition. He employed closed drainage, and on the first day about 200 cc. of serosanguineous fluid passed through the tube; about 50 cc. passed on the second and third days, after which the drainage ceased; the tube was removed on the fourth day. The lower portion of the oral end of the esophagus had to be removed on account of gangrene. Connection between the esophageal and gastric orifices was established by a rubber tube, as in Torek's case. The only further mention of this case which seems to have appeared in the literature was made by Torek,¹⁴⁶ who, in 1926, stated that the patient was then living and in good health more than a year after the operation. It is of interest that the patient was young (aged 38) and that the symptoms had existed for only six weeks.

Thoracic and Cardiac Portions (Esophagoplasty by Means of Skin or Fascia).—In 1917, Höfer and Kofler¹⁵³ described an original method of extrapleural resection of carcinoma of the thoracic portion of the esophagus with repair of the esophageal defect by skin esophagoplasty. Their work was done on the cadaver. They cut a triangular skin flap with a vertical base of 14 cm. and a length of 20 cm. The base was to the right of the vertebral column, and the flap extended over this onto the left thoracic wall. The flap was raised and reflected to the right. Then followed the removal of the portions of the right

152. Lotheissen, Georg: Zur Radikaloperation des Speiseröhrenkrebses, Arch. f. klin. Chir. **131**:200, 1924.

153. Höfer, Gustav, and Kofler, Karl: Studie über Resektion des thorakalen Oesophagus, München. med. Wchnschr. **2**:1097, 1917.

trapezius and underlying rhomboid muscles which were exposed by the reflection of the flap. The ribs exposed by this procedure were resected for 10 to 12 cm. subperiosteally, the intervening intercostal muscles cut away and the pleura and esophagus exposed. Several centimeters of the azygos vein was removed, the carcinoma freed from its attachments and the esophagus separated above and below the tumor sufficiently to allow the introduction of the skin flap under it. The apex of the flap was pulled to the left of the vertebral column as far as possible; the upper edge was brought forward on both sides of the esophagus and sutured in front; the lower edge was treated in the same manner, so that the esophagus lay in a trough of skin. The tumor bearing part of the esophagus was to be removed at a second operation, and the esophageal defect repaired by the plastic formation of a skin tube, the posterior wall of which had already been made. Höfer and Kofler stressed the importance of the exact localization of the tumor by the esophagoscope and radiography so that the flap may be outlined correctly. The right side is preferred because of the absence of the aorta. Muscle is not included in the flap, because it is prone to necrosis if separated for any length.

In 1921, Lilienthal,¹⁵⁴ unaware of the work of Höfer and Kofler, devised a similar operation and tested it on the cadaver as they had done, but he was able to apply it clinically with some success. Lilienthal used a rectangular flap, the upper border of which was the eighth interspace, the lower, the tenth rib, its outer limit the midaxillary line, and its base about 3.75 cm. from the vertebral column. Whereas Höfer and Kofler attacked the esophagus from the right side, Lilienthal did so from the left, giving as his reasons the importance of the aorta as a landmark, the greater distance from the important veins and thoracic duct, and the avoidance of the difficulty of freeing the pleural fold which crosses the median plane at this point. After freeing the esophagus, the skin flap was placed in position, lying between the esophagus and the right vagus (the left vagus was not seen), the cuticular surface next to the esophagus and the terminal end turned round it and held in position by a silk suture running from its tip to the inner part of the wall of the chest, the trough of skin thus formed to be completed into a tube by division of the pedicle later. Several days afterward the tumor was resected, and later the pedicle was divided and turned outward to meet the terminal end of the flap. The pedicle, however, showed a marked tendency to return to its normal position. Before

154. Lilienthal, Howard: Carcinoma of Thoracic Oesophagus Extrapleural Resection and Plastic: Description of an Original Method with Report of a Successful Case Without Gastrostomy, *Ann. Surg.* 74:259, 1921; Carcinoma of the Thoracic Oesophagus: Final Notes and Post-Mortem Examination in the Case Reported in the *Annals of Surgery*, September, 1921, *ibid.* 76:333, 1922.

healing finally took place by granulation, five months had elapsed since the first operation. Contraction at the upper mucocutaneous juncture necessitated the passage of sounds. The patient lived for eleven months after being dismissed from the hospital. A tracheo-esophageal fistula, caused by recurrence of the growth, and terminal pneumonia were the cause of death.

Lilienthal mentioned having on four occasions, explored the mediastinum for carcinoma of the esophagus; in every case, the tumor had extended beyond the wall of the viscus. Three of the patients died of mediastinitis through injury to the esophagus during attempts to isolate it. In the fourth case, the cause of death was unknown.

In 1921, Budde,¹⁵⁵ working on the cadaver with a view to replacement of the resected part of the esophagus, built a pedicled tube of skin, fascia and muscle around a glass rod. Part of the thoracic portion of the esophagus was then resected extrapleurally and the tube implanted between the cut ends.

In 1922, Allen¹¹⁷ resected a small piece of the thoracic portion of the esophagus and repaired the defect with fascia lata. He performed seventeen one-stage operations, with uniformly fatal results. The cause of death was empyema and mediastinitis due to leakage from the esophagus. By his two-stage method of double fascial tubes with subsequent opening of the outer tube and resection of the inner tube and that portion of esophagus inclosed by it, he performed six operations, of which four were successful. Both failures were due to empyema and mediastinitis after the first stage before the esophagus was opened.

Later, in 1925, Allen¹¹⁸ operated on the thoracic portion of the esophagus in dogs in a manner similar to that used on the cervical portion. He employed the two-stage operation to remove a section of the esophagus without actually opening its lumen at either operation, depending on the tying of ligatures, which were planted around the esophagus inside the fascial sleeve, to cause necrosis of that part of the viscus between the ligatures. In four such operations, he failed to secure sloughing in one. The other three were successful, but were followed by definite stenosis. He attempted this operation in a case of carcinoma of the thoracic portion of the esophagus, but the tumor proved to be inoperable.

Comment.—An effort has been made, by this comprehensive review of the literature, to give an idea of the wide extent to which esophageal surgery has been practiced for the removal of carcinoma, and to show that the reason it has not succeeded has not been due to the lack of either effort or ingenuity.

155. Budde, Werner: Zur Frage des plastischen Ersatzes schleimhautbekleideter Röhren: I. Urethra virilis; II. Oesophagus, Deutsche Ztschr. f. Chir. 161:1, 1921.

There are two aspects of carcinoma regarding which opinions are divergent: that of early diagnosis, and the virulence of the growth.

It is well known that exploratory operations show most carcinomas to be inoperable, and many surgeons maintain that earlier diagnosis would bring the majority of these neoplasms within the limits of operability. This opinion warrants investigation. It is noticeable in published reports of cases that patients with esophageal carcinoma rarely consult a physician at the onset of symptoms, but generally wait for months rather than weeks. Can anything be attained by the education of the laity in regard to the early symptoms of esophageal carcinoma, such as commencing difficulty in swallowing solid foods and perhaps a sense of substernal oppression or later the regurgitation of ropy mucus into the mouth, so that such patients may be seen, for example, within a week of commencement of symptoms? The answer to this question depends on two points: the actual cause of the symptoms and the virulence of the growth. With regard to the former, one can say the symptoms are due to mechanical obstruction only. This means that the growth, even when the earliest symptoms appear, must have extended sufficiently to produce obstruction. Unfortunately, carcinoma of the esophagus grows not only inward, encroaching on the lumen, but extends outward simultaneously into the surrounding tissues, laterally to involve the whole circumference and upward and downward. Carcinoma of the esophagus, therefore, will be without symptoms until it has reached considerable size and is firmly fixed to surrounding tissue, or until the contraction of fibrous tissue develops in an attempted natural cure.

The degree of malignancy is of the greatest significance. The belief that these growths are relatively benign and slow-growing has been handed down to us, based chiefly on the frequently reported inability of observers to demonstrate metastasis at necropsy; many present-day surgeons persist in holding this opinion. Abel,³ for instance said that he intends to prove that carcinoma of the esophagus is a relatively benign, mild type of malignant growth. On the other hand, the opposite view is slowly gaining ground. Souttar,¹⁵⁶ from his clinical experience, expressed the belief that carcinoma of the esophagus is of high grade malignancy, and that it fails to produce widespread secondary deposits only because death occurs early. Just as long as this problem can be discussed only on clinical grounds, there will be divergence of opinion. Broders' ¹⁵⁷ method of grading the malignancy of tumors, however, aids considerably in deciding the issue. According

156. Souttar, H. S.: Treatment of Carcinoma of the Oesophagus: Based on 100 Personal Cases and Eighteen Post-Mortem Reports, *Brit. J. Surg.* **15**:76, 1927.

157. Broders, A. C.: Squamous Epithelioma of the Lip: A Study of Five Hundred Thirty-Seven Cases, *J. A. M. A.* **74**:656 (March 6) 1920.

to the degree of differentiation of the cells, any carcinoma can be placed in one of four grades arranged in increasing order of malignancy; thus, mild, slow-growing tumors are graded 1 and the most malignant tumors are graded 4. This method, introduced in 1920, has received a fair trial, and in the hands of experts has proved to be reliable. I am indebted to Broders and Vinson¹⁰³ for allowing me to use their unpublished data concerning the malignancy of esophageal carcinoma. In a series of 220 cases of carcinoma of the esophagus observed at the Mayo Clinic, they found that more than 90 per cent of such tumors were graded 3 and 4, that is, they were of the most malignant types; cases graded 1 were not found. This is significant in considering the chance of success of surgical procedures, for it means that by the time a carcinoma has extended sufficiently to produce obstruction (at which time the earliest symptoms will appear) it will have spread beyond the limits of surgical removal, except perhaps in a few cases.

Other data compiled by Broders and Vinson strengthen this opinion and throw light on the question of metastasis. They found that in forty-two cases in which postmortem examinations were made, twenty-seven showed metastasis, whereas of the last fifteen cases of this series metastasis was found in fourteen.

Because of the anatomic structure and relationships of the esophagus, the highly malignant carcinomas of the organ, the frequent occurrence of metastasis, the danger of fatal infection and the mutilation which must always cause great shock, surgical removal of these tumors cannot be expected to be attended with any degree of success. Although a successful case may occasionally be reported, this will never justify routine surgical exploration and the attempted removal of esophageal carcinoma with its appalling mortality. The only operation which has attained even a small degree of success is extirpation of a cervical esophageal carcinoma with subsequent double flap skin esophagoplasty after the manner first introduced by von Hacker, or the single flap method of Lane¹¹⁰ and Ach.¹¹¹

Thus, it appears that only palliative measures can be applied as a routine in the treatment of patients with this disease. These include the use of radium, deep roentgen rays, diathermy, intubation, gastrostomy and dilatation. All of these methods have their advocates and their opponents, and a voluminous literature has accumulated concerning them. As this phase is nonsurgical, its discussion has been omitted as being outside the scope of the subject of this article.

DIVERTICULA

Despite the fact that the so-called esophageal (pulsion) diverticula have been proved definitely to be pharyngeal, their surgical treatment is always considered a branch of esophageal surgery. Because they are

not uncommon and because the results of their surgical treatment are highly satisfactory, it was felt that they should be considered here.

There are a few important contributions to the early literature concerning diverticula that are worthy of note. Bell,¹⁵⁸ in 1816, was the first to draw attention to their occurrence. He performed necropsy in a case in which there had been trouble with dysphagia during life and found a posteromedial pouch at the upper end of the esophagus. He likened the condition to the hernial protrusion of mucosa which occurs in the bladder in cases of urethral or prostatic obstruction. Later he suggested that the surgical treatment should consist in emptying the sac by the establishment of a fistula.

Rokitansky,¹⁵⁹ in 1840, was the first to draw attention to the occurrence of two types of diverticula and classified them from an etiologic standpoint into two groups: (1) those due to traction exerted on a portion of the esophageal wall from without, and (2) those due to pressure within. Those in the first group he called traction diverticula and those in the second pulsion or pressure diverticula. Since Zenker and von Ziemssen,¹⁶⁰ in 1877, reported on their study of twenty-seven postmortem specimens, and described the etiology, pathology, symptoms, etc., of the condition, little has been added to the knowledge of the disease except the advances in the surgical treatment. These authors stated that the radical cure of pulsion diverticula by surgical measures from without was one of vain hopes, yet they were hopeful that even this operation conducted on Lister's plan might some day be performed without danger. Such was the state of surgery fifty years ago. The monographs on diverticula by Starck,¹⁶¹ in 1900, and Rosenthal,¹⁶² in 1902, are worthy of mention as comprehensive studies on the subject.

Although Bell¹⁵⁸ surmised the pharyngeal origin of the large pulsion diverticula, and Zenker and Ziemssen proved it, for a long time it was commonly accepted that the diverticula originated in a small triangular area at the upper end of the esophagus posteriorly just below the inferior constrictor muscle of the pharynx where the divergence of the esophageal musculature caused a weak spot. Keith¹⁶³ and others, however, have definitely pricked the bubble of the Lainer-Hackermann triangle, as this area is called, and have proved beyond question that

158. Bell, Charles: *Surgical Observations*, New York, Longmans, Greene & Company, 1816, p. 64.

159. Rokitansky, C., quoted by many authors.

160. Zenker, F. A., and von Ziemssen, H.: *Krankheiten des Oesophagus in Ziemssen: Handbuch der speciellen Pathologie*, Leipzig, 1887, vol. 7, p. 1.

161. Starck, H.: *Die Divertikel der Speiseröhre*, Leipzig, 1900.

162. Rosenthal, Werner: *Die Pulsions-divertikel des Schlundes: Anatomie, Statistik, Ätiologie*, Leipzig, Georg Thieme, 1902, p. 142.

163. Keith, Arthur: *Diverticula of the Alimentary Tract of Congenital or of Obscure Origin*, Brit. M. J. 1:376, 1910.

these diverticula are formed by the evagination of the mucous membrane through the posterior pharyngeal wall between the upper and lower parts of the inferior constrictor muscle, the main function of the former being to seize the bolus of food and force it into the esophagus, while the latter acts as a sphincter to the upper orifice of that viscus. Such diverticula are, therefore, true sacculi.¹⁶⁴

Traction diverticula are usually found on the anterior wall of the esophagus near the bifurcation of the trachea, and they usually originate from a localized adhesion of the esophageal wall to the surrounding parts, sometimes the result of inflammation of one of the bronchial glands. The walls of the diverticula consist of all the coats of the esophagus, and they are therefore true diverticula.¹⁶⁴ They rarely give rise to clinical symptoms, although occasionally they may become enlarged, the increase in size being due to the arrest of food in the diverticulum and the gradually increasing pressure resulting therefrom. Oekonomides¹⁶⁵ gave the name of "traction-pressure diverticulum" to this condition.

Sauerbruch¹⁶⁶ reported a case in which a traction diverticulum had ruptured into the lung, causing abscess and the formation of fistula which necessitated operation. Ordinarily, however, such diverticula do not require surgical intervention.

The several methods of choice in the surgical treatment of pulsion diverticula (sacculi) are: extirpation in one or two stages, invagination and diverticulopexy (sacculopexy). Apart from the local operative measures, however, the preoperative preparation is important and consists of thorough oral hygiene and the lavage of the sac with mild antiseptic solutions. Some surgeons recommend preliminary gastrostomy in elderly and debilitated patients.

The earliest recorded surgical assault on a pharyngeal diverticulum was that of Nicoladoni¹⁶⁷ in 1877. His procedure consisted in opening the sac and establishing a fistula, thus putting into practice Bell's suggestion. The patient died from pneumonia six days after the operation. Shortly afterward a few surgeons attempted to remove radically these protrusions by the one-stage method, the essentials of which are the exposure and separation of the sac and its removal by cutting through the neck. The surgical approach to a diverticulum is exactly the same as that employed in cervical esophagotomy, the incision usually being

164. Morison, Rutherford, and Saint, C. F. M.: *An Introduction to Surgery*, ed. 2, Bristol, John Wright & Sons, 1926, p. 354.

165. Oekonomides, G.: *Ueber chronische Bronchialdrüsen-affectionen und ihre Folgen*, Basle, F. Riehm, 1882, p. 71.

166. Sauerbruch, F.: *Oesophagusdivertikel*, *Zentralbl.f.Chir.* 54:1508, 1927.

167. Nicoladoni, K.: *Ein Beitrag zur operativen Behandlung der Oesophagus-divertikel*, *Wien. med. Wchnschr.* 27:605 and 654, 1877.

along the anterior border of one or the other sternomastoid muscle, usually the left, because the majority of these pouches protrude on that side. C. H. Mayo,¹⁶⁸ however, advocated incision in the line of the natural crease of the neck, one-third being behind the anterior border of the sternomastoid. The sac is exposed by dissecting deeply between the carotid sheath laterally and the trachea and thyroid gland medially. After it has been separated from the surrounding structures by gentle blunt dissection, it is severed through its neck, usually between clamps or ligatures. The treatment of the stump then remains a matter of choice, but ordinarily interrupted sutures inverting the mucous membrane are used and followed by a further line of suture through the musculature. Although this operation is apparently ideal from the technical standpoint, it has a disadvantage which, although sometimes overcome, may prove fatal. Because of the absence of a serous coat, the line of suture is relatively slow in healing, and so the possibility of leakage through the sutured pedicle must always be considered and a drain inserted. Leakage will cause infection which is likely to spread down the fascial planes of the neck into the mediastinum, with fatal results.

Niehans,¹⁶⁹ in 1884, was the first surgeon to perform a one-stage operation for the removal of a diverticulum. The patient had a goiter as well. Niehans first removed the goiter, and after fifteen days, the symptoms not being relieved, excised the diverticulum with thermocautery between two ligatures. The patient was fed by stomach tube for a few days, and on the eighth day drank milk which flowed out of the cervical wound. Hemorrhage from the superior thyroid artery caused death on the twenty-fourth day after the removal of the sac.

In 1892, von Bergmann¹⁷⁰ reported the first successful extirpation of a diverticulum (6 cm. long), although a fistula persisted for several months. Kocher¹⁷¹ reported two cases in 1892. In both, operation was successful; although temporary fistula developed in one case, the wound in the other case healed by primary intention. In 1893, Dugge,¹⁷² in reporting a fatal case in which operation was not performed, commented on the small number of cases reported; he succeeded in finding only twelve cases in the literature of the six years preceding

168. Mayo, C. H.: *Diagnosis and Surgical Treatment of Esophageal Diverticula: Report of Eight Cases*, *Ann. Surg.* **51**:812, 1910.

169. Niehans, quoted by Girard: *Cong. franç. de chir.* **10**:392, 1896.

170. Von Bergmann, E.: *Ueber den Oesophagusdivertikel und seine Behandlung*, *Arch. f. klin. Chir.* **43**:1, 1892.

171. Kocher, Theodor: *Das Oesophagusdivertikel und dessen Behandlung*, *Cor.-Bl. f. Schweiz. Aerzte* **22**:233, 1892.

172. Dugge, Carl: *Ein Fall von Oesophagus-Divertikel*, *München. med. Wehnschr.* **40**:529, 1893.

1893. Since that time, the number reported has increased continually. In 1903, Butlin¹⁷³ reported eight cases in which he had operated during the preceding ten years. In 1910, Stetten¹⁷⁴ reviewed all the cases he could find in the literature up to that time, and his statistics throw some light on the results of surgical measures in this sphere. In a group of sixty patients, fifty were cured and ten died, a mortality of 16.6 per cent. In a group of forty-eight patients on whom the one-stage operation was performed, the mortality was 18.7 per cent.

In 1918, Judd¹⁷⁵ reported a series of 35 cases from the Mayo Clinic with only 2 deaths. Two years later¹⁷⁶ he reported an additional 17 cases with only 1 death, making 52 cases in all. In 1923, C. H. Mayo¹⁷⁷ stated that the total number of patients operated on at the clinic had reached 74 without further mortality. In 1921, Deis¹⁷⁸ noted 134 cases in the literature; in 88 of these, the one-stage operations had been performed with 10 deaths, a mortality of 11.3 per cent, which is below that reported by Stetten for similar cases. In 22 of the cases reviewed by Deis, the two-stage operation had been performed without deaths.

The two-stage method was introduced by Goldmann,¹⁷⁹ in 1909, its purpose being to minimize the danger of spreading infection along the fascial planes of the neck consequent on leakage from the diverticular pedicle. By this method the sac, after being freed, is brought out into the operative wound and left there for about two weeks, during which time granulations form and wall off the fascial planes of the neck. The sac is then removed and the neck sutured. Since its inception by Goldmann, the two-stage method has been widely adopted and also modified in different ways by various surgeons. Goldmann, after freeing the sac, tied the pedicle with a silk ligature, packed a tampon around the sac and closed the wound in the skin, leaving a small opening for the removal of the tampon. The tampon was removed and the sac cut off a few days later. A fistula formed and drained for two months. Deis¹⁷⁸ was of the opinion that allowing the necrotic

173. Butlin, H. T.: An Account of Eight Cases of "Pressure-Pouch" of the Oesophagus Removed by Operation, *Brit. M. J.* **2**:64, 1903.

174. Stetten, DeWitt: The Radical Extirpation of Pharyngo-Oesophageal Pressure Diverticula, *Ann. Surg.* **51**:300, 1910.

175. Judd, E. S.: Esophageal Diverticula, *Surg. Gynec. Obst.* **27**:135, 1918.

176. Judd, E. S.: Esophageal Diverticula, *Arch. Surg.* **1**:38 (July) 1920.

177. Mayo, C. H.: Treatment of Diverticulum of the Esophagus, *Ann. Surg.* **77**:267, 1923.

178. Deis, Kurt: Die Behandlung der Zenker'schen Pulsionsdivertikel der Speiseröhre, *Beitr. z. klin. Chir.* **123**:623, 1921.

179. Goldmann, E. E.: Die Zweizeitige Operation von Pulsionsdivertikeln der Speiseröhre, *Beitr. z. klin. Chir.* **61**:741, 1909.

sac to separate by itself after ligating its neck is a safe procedure. Von Beck¹⁸⁰ also recommended this method, and reported seven cases with five successes; two patients died from pneumonia. C. H. Mayo,¹⁷⁷ after delivering the sac into the wound, sutures its neck to the sternomastoid or to the platysma muscle with a few interrupted catgut sutures, and the wound in the neck is closed around the neck of the sac. Ten or twelve days later the sac is again freed, then excised and the opening in the esophagus and the wound in the neck closed. Judd¹⁷⁵ illustrated this method. Murphy¹⁸¹ advocated twisting the sac, packing around it, and later amputating it with suture of the pedicle. Wilkie's¹⁸² method offers still greater protection against the danger of cellulitis and mediastinitis. After the sac is freed, the margins of skin are sutured to its body. The second stage, performed several days later, consists of incising the base of the sac down to the submucous plane and separating the mucosa by blunt dissection for about 5 cm. from the surface of the skin. The free edges of the mucosa are then united by a roll-in suture of chromic catgut and further invaginated by interrupted sutures. The stump is allowed to retract and the wound in the skin is partially closed by sutures. Wilkie reported two cases; in the first case the wound was dry in less than three weeks, and in the second a small fistula persisted for about five weeks.

Although the two-stage method is the more popular, the one-stage method still has its advocates. In 1910, Stetten¹⁷⁴ declared that the method of Goldmann did not require serious consideration and reported a case of his own in which the patient left the hospital with the wound completely healed sixteen days after the one-stage operation. In 1922, Bensaude and Grégoire,¹⁸³ also expressed belief that the one-stage operation is best and that the two-stage operation means taking unnecessary precautions. C. H. Mayo,¹⁷⁷ however, stressed the advisability of the two-stage operation if a large pouch is present, particularly if it extends down into the thorax. Recent reports by Lahey,¹⁸⁴ and by Crile and Dinsmore¹⁸⁵ showed excellent results obtained by the two-stage method.

180. Von Beck, quoted by König: *Deutsche med. Wchnschr.* 1:719, 1922.

181. Murphy, J. B.: *Diverticulum of Esophagus: Conservative Treatment*, *Surg. Clin. Chicago* 5:391, 1916.

182. Wilkie, D. P. D., and Hartley, J. N. J.: *Pharyngeal Diverticulum and its Surgical Treatment, with a Record of Two Cases*, *Brit. J. Surg.* 10:81, 1922-1923.

183. Bensaude, R., and Grégoire: *Diagnostic et traitement des diverticules oesophagiens*, *Arch. d. mal de l'app. digestif.* 12:145, 1922.

184. Lahey, F. H.: *Oesophageal Diverticula*, *Boston M. & S. J.* 188:355, 1923.

185. Crile, G. W., and Dinsmore, Robert: *Diverticula of the Esophagus*, *S. Clin. N. Amer.* 4:863, 1924.

In 1896, Girard¹⁸⁶ treated two patients successfully by obliterating the cavity of the sac by invagination. By invaginating the sac by purse-string sutures, repeated as many times as is deemed necessary, its cavity is obliterated without being opened. The inverted sac either atrophies or sloughs off. Although this operation has the advantage of eliminating every possibility of infection, its disadvantage is that the polypoid projection produced by the inversion of the sac may, if large enough, produce occlusion of the pharyngeal lumen. This, then, would seem to limit the operation to small sacculi. There remains the question of recurrence after this operation. In 1912, Waggett and Davis¹⁸⁷ reported a case in which the former had operated by Girard's method with apparent success. Ten months after the operation, the patient said that after sneezing violently he felt "something break" in his neck. A diagnosis of reexpansion of the invaginated sac was made and operation undertaken. It was found that the diverticulum had much the same appearance as before the first operation. Radical extirpation by the one-stage method was undertaken with success, the wound healing by first intention. Bevan,¹⁸⁸ however, operated on what was evidently a large sac, and if inversion by repeated purse-string suture had been carried out, it is probable that pharyngeal occlusion would have resulted. To overcome this difficulty he used purse-string sutures for the outer part of the sac, but he reefed the inner part with longitudinal sutures, leaving the sac compressed against its attachment. In a later article,¹⁸⁹ he described a modification of this method for use with a large diverticulum. He first cuts through the middle of the sac by clamp and cautery, and after removing the outer part invaginates the remaining inner part. Von Beck¹⁹⁰ also tried the invagination method, with success. Besides being adaptable to cases of small diverticula, it is also useful if the patient is old and debilitated.

Diverticulopexy appears to have found a definite place in surgical treatment for pharyngeal diverticulum. The procedure was first proposed by Schmid¹⁹⁰ in 1912, who, on the cadaver, fixed the bottom of the sac at a higher level than its neck, the sac not being opened. This

186. Girard, C.: *Du traitement des diverticules de l'oesophage*, Cong. franç. de chir. **10**:392, 1896.

187. Waggett, E. B., and Davis, E. D.: *A Case of Pharyngeal Diverticulum*, *Lancet* **1**:786, 1912.

188. Bevan, A. D.: *Pulsion Diverticulum of the Esophagus: Cure by the Sippy-Bevan Operation*, *Surg. Clin. Chicago* **1**:449, 1917.

189. Bevan, A. D.: *Diverticula of the Esophagus*, *J. A. M. A.* **76**:285 (Jan. 29) 1921.

190. Schmid, H. H.: *Vorschlag eines einfachen Operations-verfahrens zur Behandlung des Oesophagusdivertikels*, *Wien. klin. Wchnschr.* **25**:487, 1912.

operation was first practiced on the living subject by Hill ¹⁹¹ in 1918. The sac was dissected free and the fundus stitched to the left side of the inferior constrictor muscle, with at least temporary relief of symptoms. König ¹⁹² fixed the sac to the hyoid bone with success.

In 1922, Van den Wildenberg ¹⁹³ reported that he had had recourse to diverticulopexy with complete success seven times. In four cases, he performed only this operation. In the remaining three he used it as a first stage, excising the pouch afterward at periods varying from eight days to three months. The second operation proved to be much more simple than the first, as the sac was found at once and only a small incision was needed. Diverticulopexy is not a radical procedure and Van den Wildenberg advised its use only as the first operation of a two-stage procedure; he further stressed this point in a later communication ¹⁹⁴ as a result of one case of recurrence after the operation. In one case, Hautant, ¹⁹⁵ besides performing diverticulopexy, ligated the neck of the pouch, his object being to prevent the reflux of food into its cavity, notably in postoperative vomiting. Deglutition took its normal course at once. One might think that there would be danger of sepsis from decomposition in this closed cavity. Hautant's patient, however, had enjoyed excellent health for six months at the time of report.

In summarizing the present status of the surgical treatment of pharyngeal sacculi one might say that the two-stage method can be done with so little risk that it has been adopted practically universally. Van den Wildenberg ¹⁹⁴ has introduced sacculopexy as the first stage in two-stage removal. Statistics show that the one-stage method, although ideal from the technical standpoint, means unnecessary risk.

Invagination and sacculopexy have the disadvantage of not being radical operations. The former, however, is well suited for small sacculi, and although large ones can be treated in this manner, this procedure is not likely to be preferred to extirpation. Sacculopexy, by its simplicity, the absence of the risk of sepsis and because of the results already attained by this method, seems likely to become a more popular operative procedure as time goes on. It would seem to be ideal for old and debilitated patients.

191. Hill, William: Pharyngeal Pouch Treated by Diverticulopexy, *Proc. Roy. Soc. Med.* **11**: (Sect. Laryngol.) 60, 1918.

192. König, Fritz: Zur Operation des Oesophagusdivertikels, *Deutsche med. Wchnschr.* **1**:719, 1922.

193. Van den Wildenberg: Diverticules dans l'oesophage, *Arch. franco-belges d. chir.* **25**:526, 1922.

194. Van den Wildenberg: Quatre nouveaux cas des diverticules oesophagiens opérés et guéris, *Ann. d. mal. de l'oreille, du larynx.* **46**:222, 1927.

195. Hautant, A.: Diverticule de l'oesophage guéri par diverticulopexie, *Ann. d. mal. de l'oreille, du larynx.* **43**:1016, 1924.

EXPERIMENTAL INVESTIGATION

The object of the experimental work undertaken was to obtain if possible a successful method of suture for end-to-end anastomosis of the esophagus, at first after simple division, and, if this proved satisfactory, after resection.

The difficulties which beset the surgeon in operating on the esophagus have been discussed. They exist because of the unique anatomic structure and relationships of the viscus. In my earliest experiments on the anastomosis of the divided organ, I was particularly impressed with the poor nature of the blood supply. Fatal cellulitis and mediastinitis were the outcome, and necropsy showed not only sloughing of the cut ends of the esophagus constricted by the sutures, but discoloration of the mucous membrane for several centimeters above and below the level of division which corresponded to the length of the esophagus necessarily isolated for the performance of the operation. As these experimental operations had been carried out with the usual aseptic precautions, it was felt that the primary factor causing the ensuing fatal infections was not the contamination of the surrounding tissues with esophageal secretion at the time of operation, as many authors seem to believe, but the sloughing at the line of anastomosis due to constriction of its blood supply by the sutures, with resultant leakage of infective esophageal secretion.

This led me to investigate the blood supply to the esophagus in the dog. After several unsuccessful attempts with prussian blue and carmine gelatin injections, it was decided that the most satisfactory method would be the injection of a radiopaque medium. That used was a mixture of barium sulphate and gelatin, made up according to the directions given by Gross¹⁹⁶ as follows:

Soak 300 Gm. of fine French gelatine for two hours in 1,200 cc. of distilled water. To this add 1,000 Gm. of finely powdered barium sulphate, 500 cc. of distilled water, and 2 Gm. of thymol. Heat over a water bath until the gelatine dissolves and stir until the whole mass becomes a homogeneous milky fluid. Filter through two layers of Victoria lawn.

The specimen for injection was obtained in a manner similar to that used by Demel¹⁹⁷ in his work on the blood supply to the human esophagus. A recently killed dog was used. A median line incision was made which extended from the chin to the pubis, the skin was reflected widely on each side and the sternum and chondral parts of the ribs removed. The tongue was severed from its attachments, the posterior

196. Gross, Louis: *The Blood Supply to the Heart in its Anatomical and Clinical Aspects*, New York, Paul B. Hoeber, 1921, vol. 16, p. 171.

197. Demel, Rudolf: *Die Gefäßversorgung der Speiseröhre: Ein Beitrag zur Oesophaguschirurgie*, Arch. f. klin. Chir. 128:453, 1924.

pharyngeal wall cut through, and the whole of the cervical viscera removed. The ascending part of the aorta was cut between ligatures and the heart removed; each lung was removed by cutting through the hilum just distal to a ligature and through the pulmonary ligament. By the removal of the heart and both lungs, the vascular bed to be injected was considerably diminished in size. The parietal pleura was incised on both sides about 2.5 cm. from the vertebral column. The intercostal vessels were ligated and cut from above downward to the level of the diaphragm, which was then separated from its costal and vertebral attachments. The hepatic artery was ligated and cut and the gastrohepatic ligament divided; the first part of the duodenum was cut between ligatures; the splenic artery was ligated and cut close to the spleen, and the branches of the gastro-epiploic arteries descending into the greater omentum were ligated and the omentum divided. The superior mesenteric, inferior mesenteric and renal arteries were then ligated and cut; the lumbar branches of the aorta were dealt with in the same manner and the aorta itself was severed just above its bifurcation.

In this way a specimen was obtained consisting of the whole length of the esophagus, the trachea, stomach and diaphragm, together with all the arteries from which the esophagus receives its blood supply.

A cannula was tied into the lower end of the aorta and the vascular bed of the specimen was washed out thoroughly with water injected into the cannula by a syringe. In order to render the vascular bed water-tight it was necessary to ligate such arteries as the internal and external carotids, the subclavians, the vertebrales, the transverse cervical and scapular arteries, the internal mammary arteries and any others through which water was seen to escape during the washing process.

The specimen was now ready for injection and was placed in the dish containing hot water. The injection apparatus was rendered as air-tight as possible, and when the valve on top of the oxygen tank was opened, gas passed into the carboy. The pinchcock was opened slightly; the mercury in the limbs of the manometer immediately showed a difference of from 10 to 20 mm.; the effect of this pressure acting on the surface of the injection medium was to force the latter out of the bottle, into the rubber tube to be connected with the cannula in the specimen. Before this connection was made, however, the mixture of barium sulphate and gelatin was allowed to run out of the rubber tube, as otherwise the air contained in the tube would be forced into the specimen in front of the injection medium which would then be unable to fill the vascular bed completely. As soon as the connection was made, the medium began to flow into the aorta and its branches. The pinchcock was opened gradually until the mercury in the limbs of the manometer showed a difference in height of 200 mm.,

and the medium was seen to fill the finer branches of the vascular bed. This pressure was maintained for one hour.

The aorta was then ligated and the cannula withdrawn. The specimen was placed in 10 per cent solution of formaldehyde for twenty-four hours, at the end of which time the injected barium sulphate and gelatin had solidified and roentgenograms were taken. Figures 1 and 2 show specimens prepared by this method. Several other specimens were injected and photographs taken. One specimen after injection was cleared by the Spalteholz method which consists of dehydration by



Fig. 1.—Roentgenogram of injected specimen.

alcohol, and then immersion in benzene and synthetic oil of wintergreen. The specimen was first placed in 40 per cent alcohol and changed every two days into an alcohol of 10 per cent additional strength, ending with immersion in absolute alcohol for four or five days. Next the specimen was immersed in benzene for two days, after which it was placed in oil of wintergreen. Clearing commenced almost immediately and continued until fine arterial twigs could be seen clearly. Oil of wintergreen forms the medium in which such a cleared specimen may be mounted permanently.

Figures 3 to 9 represent only a small part of the material which was studied and which was found to show the following points of interest:

1. The roentgenograms showed the poverty of the blood supply to the esophagus. This is apparent when the small amount of injection medium capable of filling the arteries of the esophagus is contrasted with the large quantity necessary to fill those of the stomach.

2. The blood supply is segmental. Most of the arteries divide into ascending and descending branches, and those of one particular segment anastomose with the arteries supplying the segments above and below.

3. The anastomotic network between the arteries of adjacent segments is scanty.



Fig. 2.—Roentgenogram of injected specimen. Cervical portion of trachea removed.

4. The arteries on entering the wall of the esophagus quickly pass into its submucous layer and there ramify. Microscopic sections of an esophagus, the arteries of which have been injected, show this layer to be by far the most vascular.

5. According to the distribution of its blood supply, the esophagus may be divided into the following segments: cervical, upper thoracic, middle thoracic, lower thoracic and abdominal.

The cervical segment is the most poorly supplied with blood of all the segments of the esophagus. Its upper and middle parts derive their blood supply from descending branches of the thyroid artery (this

artery corresponds to the superior thyroid artery in man and alone supplies the gland, there being no inferior thyroid artery in the dog). The lower part of this segment is the most vascular and receives its blood supply from ascending branches of the artery supplying the upper thoracic segment. Occasional twigs are given to the middle part of the cervical segment by the common carotid arteries.

In the esophagus of man, Demel found that three constant branches from the inferior thyroid artery supplied the lower part of the cervical segment, the first of these originating from the center of the ascending

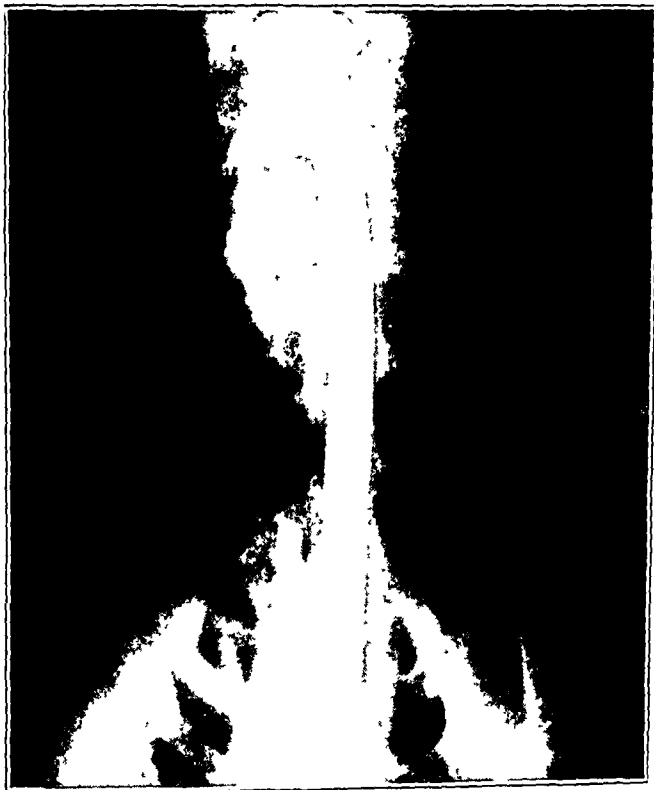


Fig. 3.—Roentgenogram showing large-sized stomach tube in esophagus of dog (dog 1, table) twenty-two days after operation. The tube passed down without any difficulty.

portion, the second from the median bend and the third from the lower ascending portion close to the subclavian artery.

The upper thoracic segment is the part of the esophagus at the level of the innominate artery. From about the middle of the artery a constant tracheo-esophageal branch arises which soon divides into two branches, one supplying the esophagus and the other the trachea. The former divides into ascending and descending branches. Those which ascend anastomose with the descending branches from the thyroid artery

and with those from the common carotid when present. The descending branches anastomose with branches of the arteries which supply the middle thoracic segment. Demel did not find this tracheo-esophageal artery in his specimens from human subjects. Its place is taken apparently by the esophageal branches of the inferior thyroid.

The middle thoracic segment corresponds to the level of the bifurcation of the trachea. It receives its blood supply from two esophago-tracheal arteries which were found to arise either from the second



Fig. 4.—Cervical portion of esophagus removed from dog (dog 1) eighty-three days after operation; *a*, line of anastomosis.

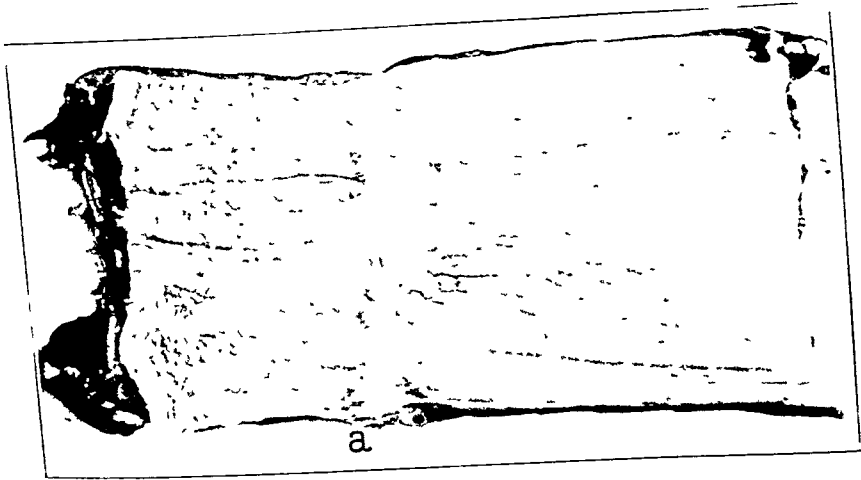


Fig. 5.—Mucosal surface of specimen shown in figure 4. The line of anastomosis, *a*, is seen as a pale transverse ridge over which the epithelium has grown completely; absence of stenosis (compare with figure 9).

intercostal artery near its origin or directly from the aorta at this level. Sometimes the arteries arise separately and at other times they spring from a common trunk only 2 or 3 mm. in length. They pass forward and downward and shortly before reaching the esophagus divide into two branches, an esophageal and a tracheal, the latter ascending to the bifurcation and the former entering the esophagus on its lateral aspects and then dividing into ascending and descending branches. The anasto-

mose above with twigs from the esophageal branch of the innominate artery and below with those from the arteries which supply the lower thoracic segment. This segment is the most vascular part of the canine esophagus. Demel found that it is also the most vascular part of the esophagus of man, which fact is of interest as the majority of esophageal carcinomas are found there.

The lower thoracic segment extends from just below the level of the bifurcation of the trachea to the diaphragm, and derives its blood supply from two arteries which arise from the third left intercostal artery near its origin or directly from the aorta at this level usually by a common trunk which is short although longer than that of the tracheo-esophageal arteries supplying the segment above. It divides into its two branches,

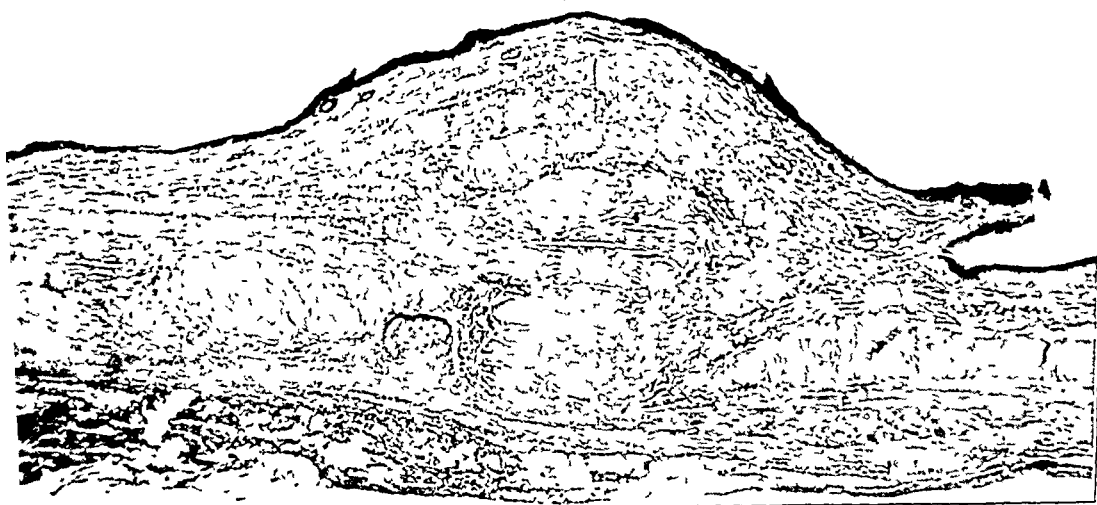


Fig. 6—Longitudinal section through line of anastomosis of specimen in figures 4 and 5, complete epithelial overgrowth; the muscular coat is thickened at this point due to the method of suture; outside the muscular coat and covered by adventitia are the remains of a silk suture encapsulated by cellular fibrous tissue.

which pass downward, forward and to the left until they reach the lateral aspects of the esophagus where they enter it and divide into ascending and descending branches. To similar arteries in specimens from human subjects Demel gave the name "*arteriores esophageae propriae*." The lowest part of this segment has the poorest blood supply of the whole length of the thoracic portions of the esophagus.

In the arrangement of the tracheo-esophageal arteries and the *arteriores propriae* as described, slight variations may occur. Their mode of origin has been commented on. Sometimes one of the branches of the tracheo-esophageal trunk will supply only the esophagus. At other times one of the *arteriores propriae* will send an ascending branch

to the bifurcation of the trachea (fig. 1). Thus, there is apparently a compensatory arrangement in this group of arteries.

The abdominal segment is the part of the esophagus below the diaphragm. It is dependent for its blood supply on small ascending twigs which arise from the left gastric and left inferior phrenic arteries near their origins. They pass upward on the esophageal wall to anastomose with the descending twigs of the arteriores propriae.



Figure 7

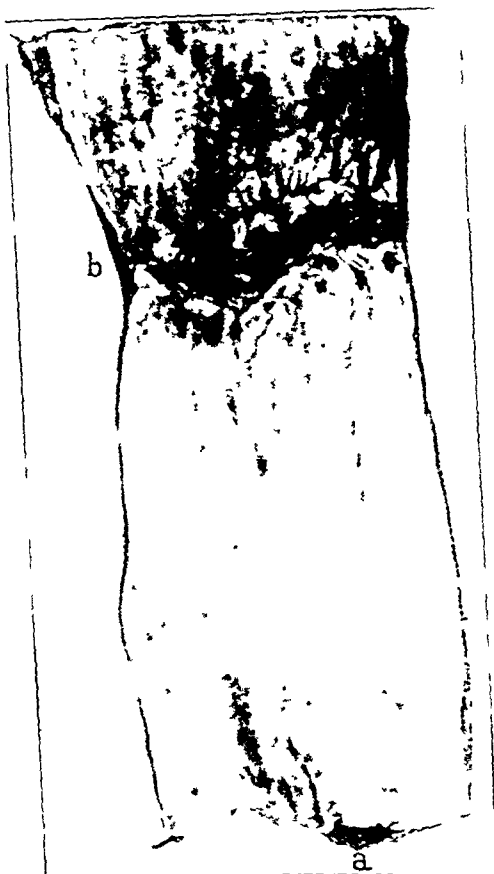


Figure 8

Fig 7—Cervical portion of esophagus distended with water; specimen removed from dog (dog 2, table) seven days after operation. Absence of stenosis, *a*, oral end, *b*, line of anastomosis

Fig 8—Mucosal surface of specimen shown in figure 7. Epithelial overgrowth has not taken place (compare with figure 5) Absence of stenosis, *a*, oral end; *b*, line of anastomosis

These investigations show that the blood supply to the esophagus in the dog closely resembles that in man (as described in detail by Demel), the only difference being the replacement of the branches from the inferior thyroid artery by those from the tracheo-esophageal branch of the innominate artery.

The ability of a suture line to hold together the two cut ends of any viscus depends primarily on the conservation of a sufficient blood supply to the line of anastomosis. These studies clearly demonstrate the poverty of the blood supply to the esophagus and in consequence show that unless special care is exercised it would be an easy matter to produce enough constriction of the blood vessels by the sutures to cause sloughing of the two cut ends, which would result in the extravasation of the esophageal secretion with fatal infection.

Other factors that would appear to contribute to success are the smallness of the suture material and the putting at rest of the organ for a reasonable time after operation so that tension on the suture line is avoided. The structure of the esophageal wall must also be taken into consideration. The muscular coat forms poor material for suture as it will easily tear. The submucous layer, on the other hand, is strong and

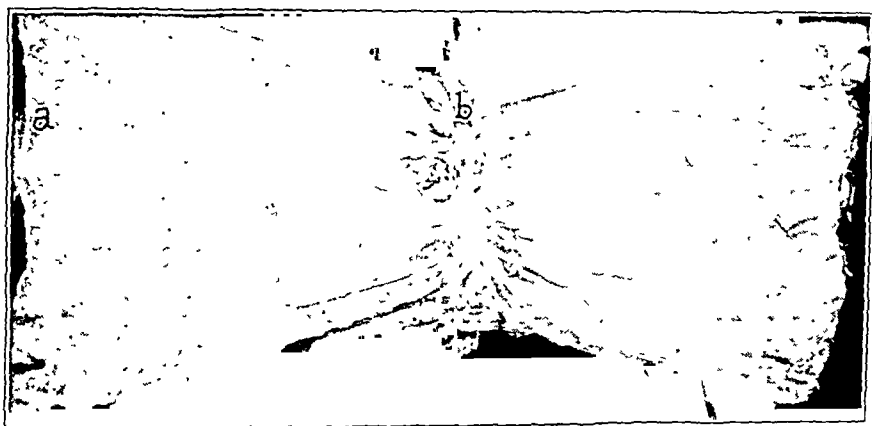


Fig. 9.—Mucosal surface of cervical portion of esophagus removed from dog (dog 5, table) thirty-six days after operation. Marked stenosis, with dilatation above the stricture. Epithelial continuity established over line of anastomosis; *a*, oral end; *b*, line of anastomosis.

its inclusion in the sutures is essential if the two cut ends are to remain in apposition. Aseptic technic with careful packing off of the divided esophagus from the surrounding tissues is a *sine qua non*. With these factors in mind, the following technic was devised for the end-to-end anastomosis of a divided esophagus:

The material used was Japanese blood vessel silk, no. 0 (which is finer and stronger than the thinnest catgut) on a fine straight needle, no. 12, about 1.25 cm. long.

The anastomosis was made by two rows of sutures. The inner row consisted of eight or nine interrupted inverting mattress sutures, spaced evenly around the circumference and passing through the whole thickness of the esophageal wall, thus including the strong submucous layer

in their grasp. The needle pierced the wall about 2 mm. from the cut edge, and each suture included about 2 mm. of the circumference in its grasp. Thus, while the blood supply to those parts of the esophageal wall caught in the sutures was constricted when they were tied, that of the remaining greater part of the circumference was unharmed. The outer row was a continuous suture passing only through the muscular coat and avoiding the submucosa where the vessels ramify. This outer row inverted the inner row and made the anastomosis water-tight.

It was decided first to attempt division at different levels of the esophagus, beginning with its cervical part, to ascertain the effect, if any, of the varying blood supply on the anastomosis. The operative procedure on this part of the esophagus was carried out as follows:

The anterior part of the neck was shaved and the animal anesthetized in the cabinet ordinarily used for this purpose at the Institute of Experimental Surgery and Pathology.¹⁹⁸ After the animal had been properly arranged on the operating table, the anesthetic was administered by the intratracheal method. The part shaved for operation was then treated with two coats of 2 per cent iodine in ether and draped with sterile towels. A median line incision was made which extended from the cricoid cartilage to the jugular notch. After hemostasis had been accomplished, sterile towels were clipped to the edges of the wound, thus excluding the skin from the area of operation. The incision was continued down to the trachea in the median line between the hyoid depressor muscles. The pretracheal fascia having been cut through, a finger was inserted backward along the left side of the trachea and hooked around the esophagus which was then brought up into the wound. The recurrent laryngeal nerves which are adherent to the esophagus were stripped off from it and the viscus isolated by blunt dissection. This method of approach to the esophagus is much easier than that between the sternomastoid muscle laterally and the hyoid depressor muscles medially. Enough of the esophagus was isolated to admit the application of two intestinal clamps between which the esophagus was to be divided, the required length being about 5 cm. These clamps were used only to occlude the lumen of the esophagus and so prevent the escape of secretion into the field of operation from either above or below. The pressure exerted by them was not sufficient to injure the blood supply. After the clamps were applied, the esophagus was thoroughly packed off in a manner similar to that used when gastro-enterostomy is to be performed. The part of the viscus between the clamps was then cut through by scalpel or straight scissors, and the ends turned upward and thoroughly wiped. The technic which has been described for end-to-end

198. Mann, F. C.: Anesthesia in Experimental Surgery, *Am. J. Surg.* 34: (Anesthesia Supplement) 73, 1920.

anastomosis of the cut ends of the esophagus was then applied. Four or five interrupted inverting mattress sutures were inserted through the posterior half of the circumferences of the cut ends, the clamps were held close together to take tension off the sutures, which were then tied. The anterior halves of the circumferences were then drawn together by four or five similar sutures, each being tied before the next was inserted. The clamps were taken off at this stage. The second row, a continuous suture inverting the first, was begun at the center of the anterior part of the line of anastomosis. Traction toward the left was put on the short end while the suture was continued to the right. Each bite of the needle included as much of the esophageal muscular coat as seemed necessary to prevent the cutting through of the silk. When a point about half way around the circumference was reached, the needle was passed under the esophagus to the left side. Traction was then exerted on the short end toward the right and the suture continued from left to right until the starting point was again reached. In this way the entire circumference of the esophagus was sutured with ease. This method of performing the outer continuous suture is technically easier than putting in its posterior half before the introduction of the mattress sutures, as in gastro-enterostomy.

The esophagus was then replaced in its bed; the hyoid depressor and sternomastoid muscles fell into place; three or four interrupted catgut sutures were used to draw together the deep cervical fascia, and the skin was closed by a continuous suture of buttonhole-twist thread. Hemorrhage during the operation was not great.

The postoperative treatment is of great importance in the success of the operation. It consisted in placing the esophagus at rest for seven days by not giving any food or water by mouth during this period. Water balance and nutrition were maintained by 10 per cent dextrose solution in physiologic solution of sodium chloride administered intravenously in quantities varying from 200 to 350 cc. each day, according to the weight of the dog. At the end of this time the animal was allowed a mixture of milk and syrup for another period of seven days, after which ordinary food was given.

I performed six operations by this method on the cervical portion of the esophagus at different levels (table). Stricture occurred in two of the animals, probably because too much of the circumference of the esophageal wall was grasped by some or all of the mattress sutures, an imperfection in technic which can be remedied with care.

In only one of the six experiments did infection supervene. In the remaining five, the blood supply to the line of anastomosis was conserved sufficiently to prevent sloughing.

In the experiment in which sloughing of part of the line of anastomosis occurred, the operation was performed on the most vascular (lower) region of the cervical part of the esophagus; since a successful operation was performed later in the same region, the failure can be attributed only to faulty technic.

Four of the operations in which sloughing did not occur were performed on the least vascular (upper and middle) regions of the cervical part of the esophagus.

Results of the Division of the Suture of the Cervical Portion of the Esophagus

Dog	Date of Operation	Level of Division of Cervical Portion of Esophagus	Results		Comment
			Infection	Stenosis	
1	12/6/27	Middle	—	—	Animal in good health to time of death (27-28), eighty-four days after operation; large sized stomach tube passed down esophagus without difficulty twenty-two days after operation
2	12/16/27	Upper	—	—	The plethysmograph had been applied to the spleen previously; the animal died suddenly seven days after operation; necropsy did not reveal the cause of death, a few adhesions were found around the esophagus at a level of the line of anastomosis, stenosis was absent
3	12/16/27	Lower	±	—	At operation this part of the cervical portion of the esophagus was found to be noticeably more vascular than the upper and middle parts (in agreement with observations in investigation of the blood supply to the esophagus); swelling of the neck fifth day after operation; 150 cc. of foul-smelling pus evacuated; animal died the seventh day after operation; necropsy showed sloughing of the anterior half of the line of anastomosis, posterior half intact, infection of the neck remarkably localized, in spite of low level of site of operation mediastinitis was not found
4	12/20/27	Lower	—	—	Animal alive and in good health; no dysphagia
5	12/21/27	Middle	—	±	Animal swallowed only fluids up to time of death, thirty-six days after operation; necropsy showed bilateral bronchopneumonia (? aspiration), marked above stricture
6	12/21/27	Upper	—	±	Animal alive, fluids only, but swallowing

The results of these operations show that this method of suture allows for a supply of blood to the line of anastomosis plentiful enough to prevent sloughing and ensure union, even when the esophagus is divided in the least vascular regions of its cervical part.

Further experimental surgery along these lines, which will include resection of the cervical portion of the esophagus, together with division and resection of its thoracic portion, is being carried out.

SUMMARY

An outline is given of the development of surgery of the esophagus with a comprehensive survey of the literature on the subject up to the end of 1927.

The problems which have rendered surgical procedures in this sphere so difficult and which still remain to be overcome have been discussed.

They lie in the anatomic structure and relationship of the esophagus and in the risk of fatal infection of the pleura and the cellular tissue of the neck and mediastinum.

The numerous operations devised and performed for the extirpation of esophageal carcinoma have resulted in an appalling mortality.

It is pointed out that such tumors are highly malignant, that they metastasize readily, and that by the time they give rise to symptoms they usually have spread beyond the limits of surgical removal.

The various methods used for the plastic formation of a new esophagus in cases of benign cicatricial stricture believed to be impermeable are described. There is a mortality of 20 per cent in the cases reported in the literature; in addition, several operations are necessary and they require months for completion, and completion is by no means assured. These reasons render plastic operations *undesirable procedures, to be avoided by early and adequate dilation and by impressing on the patient the necessity for further dilation at stated intervals.*

It would seem, too, that plastic operations have been undertaken unjustifiably in many cases, the inability to pass the smallest sound being taken as the indication of impermeability. In nearly all such cases, however, a swallowed silk thread can worm its way through the stricture and then be used as a guide for sounds.

Pharyngeal diverticula are considered to be true sacculi and traction pouches to be true diverticula. The latter rarely require surgical treatment. The results of removal of pharyngeal sacculi by the two-stage method show that it is associated with lower mortality than the one-stage operation, and in consequence is practiced more commonly.

A method of suture which has given satisfactory results is described for the end-to-end anastomosis of a divided esophagus. The suitability of this method as a means of anastomosing the two cut ends of an esophagus after a portion of it has been resected is being investigated.

A NEW ABDOMINAL INCISION *

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The type of incision employed is one of the most important factors in the ultimate results obtained in operations on the abdomen. Sir Barkley Moynihan, in his chapter on abdominal incisions, stated that if the incision is improperly made by the free division of muscular fibers or a wilful and unnecessary severing of nerve trunks a weakened area is left in the abdominal wall, which may cause the patient distress of even greater severity than did the condition which primarily necessitated the operation. It would seem that the qualifications which should commend an abdominal incision are: that it give adequate exposure, disturb a minimum number of nerve and muscular fibers and be so placed that closure is simple, and that a minimum number of postoperative hernias follow its use.

I feel that there have been too many postoperative hernias following midline incisions or long incisions of the right rectus muscle and that a change from the old routine incision of the upper part of the abdomen should be made. I believe that the incision which I wish to present may be closed with less tension on the edges of the wound, will cut no muscles and will disturb few nerves; these are factors which should produce fewer postoperative adhesions, less abdominal pain and fewer postoperative hernias.

My experience again would lead me to believe that there are a large number of weak scars of the upper part of the abdomen following all types of incisions of the upper part of the abdomen now in use. Sloan's¹ report of weakened abdominal walls in 80 per cent of his cases coincides with my experience. In many instances there was no hernia but the abdominal wall was so thin that the constant wear and tear of a number of years, plus any slight strain, might be followed by a definite hernia. Observers, from Abel² in 1899 to the present time, have reported from 2 to 8.9 per cent of postoperative hernias. These percentages must be based on short postoperative periods of observation. My statistics would lead one to believe that the percentages, when based on five year periods of postoperative observation, are much higher.

* Submitted for publication, March 16, 1929.

1. Sloan, G. A.: A New Upper Abdominal Incision, *Surg. Gynec. Obst.* 45:678 (Nov.) 1927.

2. Abel: *Progressive Medicine*, 1899.

The rule that the frequency of hernia increases in proportion to the square of the length of the incision does not indicate as great incidence in the long incision as really exists. In the olden days, when drainage of the gallbladder was done more frequently than now, one frequently saw a short incision, approximately 3 inches (7.6 cm.) in length. One did not see many hernias or weak scars among these patients, but at the present time, when cholecystectomy plus appendectomy is in vogue, a great number of hernias occur in the long straight incisions, usually a little to one side of the rectus muscle.

The nerve supply of the rectus muscle is so situated that splitting the muscle for any distance will sever the nerve fibers and leave the inner side of the rectus devoid of nerve supply. In most of the cases in which a wide vertical splitting of the rectus fibers has been performed, atrophy of the inner side of the muscle occurs, owing to the cutting of nerves and to the dissociation of muscles and nerves at the time of the operation. One was at a loss to understand, at first, why these patients left the hospital with a fairly firm wound, and, as time passed, subsequent observations revealed a progressive thinning of the wound until a hernia developed or became imminent. Now it is realized that these developments were the result of muscle atrophy. This realization encouraged the effort to refrain from splitting the muscles if possible, and thus to conserve the nerve supply.

As Moschcowitz³ stated:

The rectus muscle is attached only anteriorly to the sheath and even here only at the three so-called lineae transversae, while its attachment to the posterior sheath is very loose and readily broken up. The lineae transversae, before mentioned, do not penetrate the entire thickness of the muscle but merely the anterior third or half.

On investigation I found these statements to be "anatomic facts," and thus I obtained the idea of rolling the muscles away from the posterior sheath, leaving it attached in its outer two-thirds to the anterior sheath, as will be described later in a drawing.

In addition, interesting investigations have been made by Professor Stopford and Mr. A. H. Southam,⁴ who describe them as follows:

We first examined the results of the incision passing through the outer third of the rectus muscle, splitting the fibers, and where two, or often more, nerves had been divided. This incision is easily and rapidly made and gives good access to most of the abdominal viscera. We found there was a very definite sensory loss, as shown by anesthesia and analgesia in the strip of skin between the scar and the

3. Moschcowitz, A. U.: Transverse Incisions in the Upper Abdomen, *Ann. Surg.* **64**:268, 1916.

4. Southam, A. H.: A Comparative Study of Abdominal Incisions, *Brit. M. J.* **1**:513 (March 22) 1924.

lineae alba. After about fifteen months, however, the sensory loss becomes negligible, as far as ordinary testing can determine, probably owing to regeneration of nerve fibers.

In all these cases there was a marked loss of function of that part of the rectus muscle lying between the point where the fibers were split and the midline. This may be fairly extensive or confined to one segment of the muscle, depending upon how many nerves have been divided. It is present from the outset and persists for a considerable period. In a few cases there was a slight bulge when coughing but for the most part the loss of muscle function could only be detected when the patient raised the head and shoulders from the couch. The functional results from the patient's point of view were excellent, and after secure suture and healing by first intention, no disability was apparent from the abdominal scar.

We next followed up the results obtained by the paramedian or rectus slide incision with outward displacement of the muscle and its nerves. In these cases, for some reason not readily explained, the sensory loss is insignificant from the start. We found that in this group the rectus muscle on the side of the scar functions normally throughout, and there is no weakness discoverable after this operation.

Sloan¹ has given some interesting and instructive information on the subject of vertical and lateral tension in an abdominal incision. By measuring the tension with spring scales attached to several forceps with lateral, transverse and "L"-shaped incisions, he found that the amount of tension increases approximately in proportion to the square of the length of the incision. In an incision 3 inches long, with the patient lightly anesthetized, there is about 30 pounds (13.6 Kg.) and in a 5 inch (12.7 cm.) incision there is about 80 pounds, (36.3 Kg.) tension. Another interesting point is that there is about thirty times as much tension from side to side on a longitudinal incision as there is from above and below on a transverse incision. The tension of the transverse incision can be lessened by a suitable posture, which has been suggested by Farr, in operating with the patient under local anesthesia.

I have found that the tension depends somewhat on the musculature of the abdominal wall. In a small woman with a thin abdominal wall, it is rarely possible to get more than from a 15 to a 20 pound (6.8 to 9 Kg.) pull on the scales when she is lightly anesthetized, while on a muscular man I have seen the scales go up as high as from 50 to 60 pounds (22.7 to 27.2 Kg.), approximating a 6 inch (15.24 cm.) incision during the time he was straining.

As to the frequency of postoperative adhesions, it cannot be stated correctly that one incision has any advantage over another, because many adhesions are due to causes far removed from the type of abdominal incision and the method of closure. I have noticed, however, that in most cases in which there was a straight, long, weak incision, or in which there was evidence of a hernia, adhesions to the parietal peritoneum were present in close proximity to the incision. From these

observations, it would seem that a strong firm scar is of primary importance in the prevention of postoperative parietal adhesions.

I shall describe a longitudinal and transverse incision that has been developed in the clinic within the past two years. It has been used forty-six times and, excepting one case in which the patient had a severe bronchopneumonia and coughed incessantly for days, has given uniform satisfaction. In this one case there was a slight separation of the transverse suture line, which was resutured immediately with a satisfactory result. This incision is based on the principle of the Kammerer incision, that of displacing the rectus muscles outward, and of the Mayo operation for the relief of umbilical hernia.

OPERATIVE PROCEDURE

A description of this incision follows:

Step 1: The incision is begun just to the left and below the ensiform cartilage. It is carried downward through the skin and fat to the median of the fascia covering the left rectus muscle. The incision is lengthened downward along the rectus muscle to within 2 or 3 cm. of the umbilicus; then it is carried straight across the midline to the right rectus muscle and downward along that muscle from 4 to 6 cm.

Step 2: The anterior surface of the left rectus muscle is cleared of fat. The fascia is also cleared well in the transverse and right rectus incisions.

Step 3: The fascia on the inner third of the left rectus muscle is split the length of the incision. A transverse incision is then made from one rectus muscle to the other. The fascia on the inner one third of the right rectus muscle is then opened.

Step 4: The muscles are rolled outward and the peritoneum opened behind the left rectus muscle. A transverse incision through the peritoneum just above the umbilicus completes the incision. This gives ample exposure for any operation in the upper part of the abdomen and allows the operator to reach and remove a retrocecal appendix in the lower right quadrant.

The following is the method of closure: The patient is placed in a flexed position. The transverse incision is first closed before the peritoneum is sutured. The suture is made after the manner of the Mayo repair of umbilical hernia, imbricating the upper with the lower flap securely with from two to three mattress sutures. The approximation of this part of the wound is facilitated by the flexed posture that has been advocated by Farr. The peritoneum of the upper part of the wound is then closed separately. The muscles are allowed to drop back in their sheaths and the aponeuroses are sutured in the usual manner.

CONCLUSIONS

A new abdominal incision is described for which the following advantages are claimed: The exposure is greater than in any incision that I have ever tried. It is easy of closure. It is a combination of a longitudinal and a transverse incision, allowing the wear and tear of years of tension on a scar line to fall on both of the recti muscles

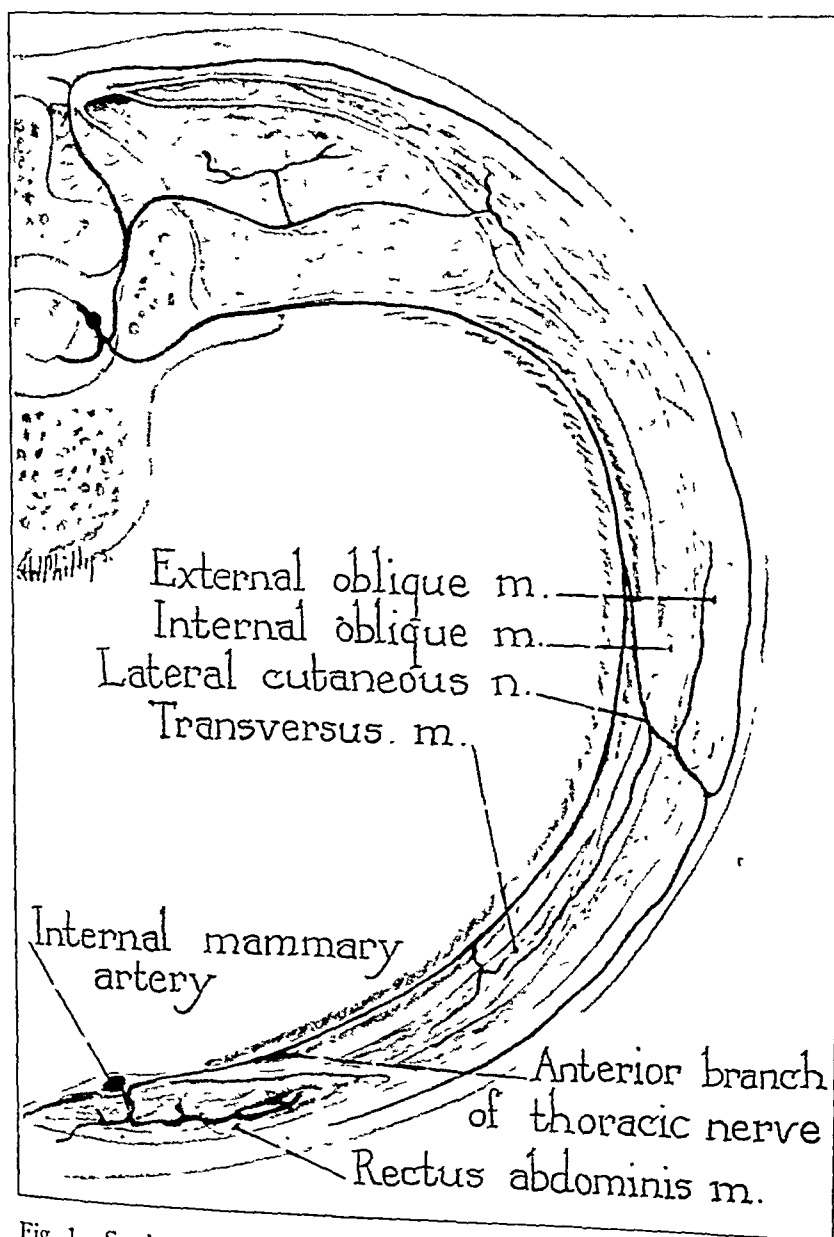


Fig 1.—Section through the lower portion of the costal arch, demonstrating the nerve supply to the rectus abdominis muscle.

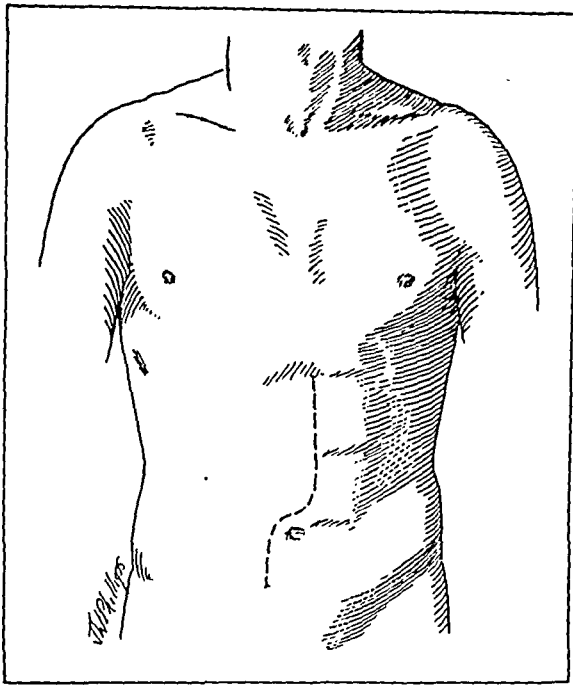


Fig. 2.—The dotted lines indicate where the incision is to be made.

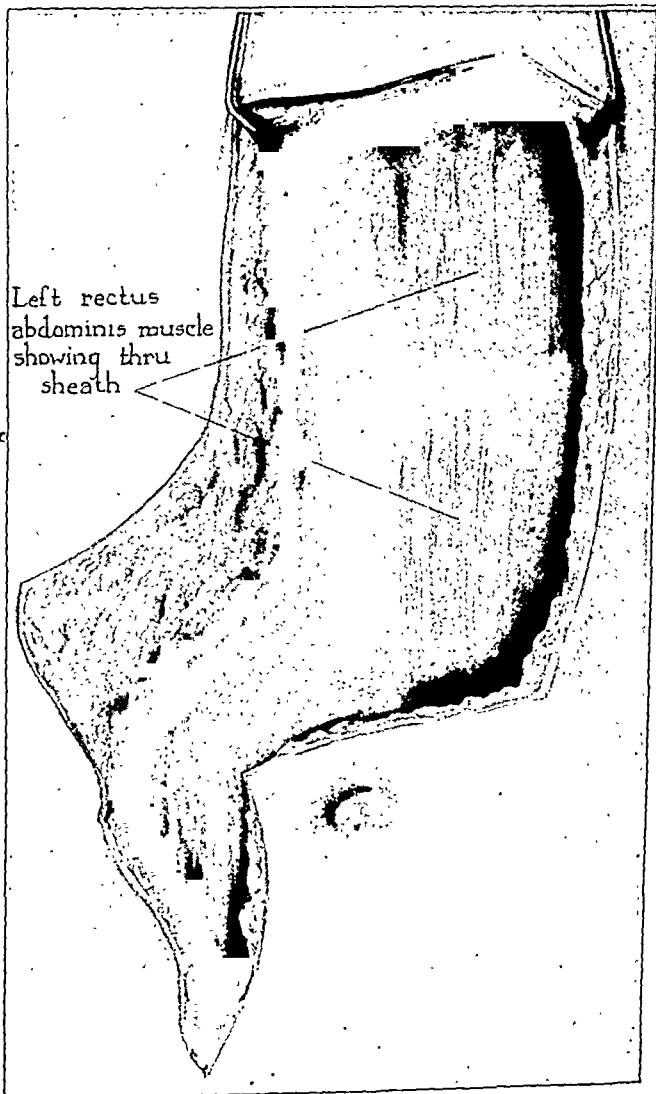


Fig. 3.—Superficial dissection, showing the right rectus muscle and the lineae transversae in the upper part of the wound, and the sheath of the right rectus in the lower part of the wound.

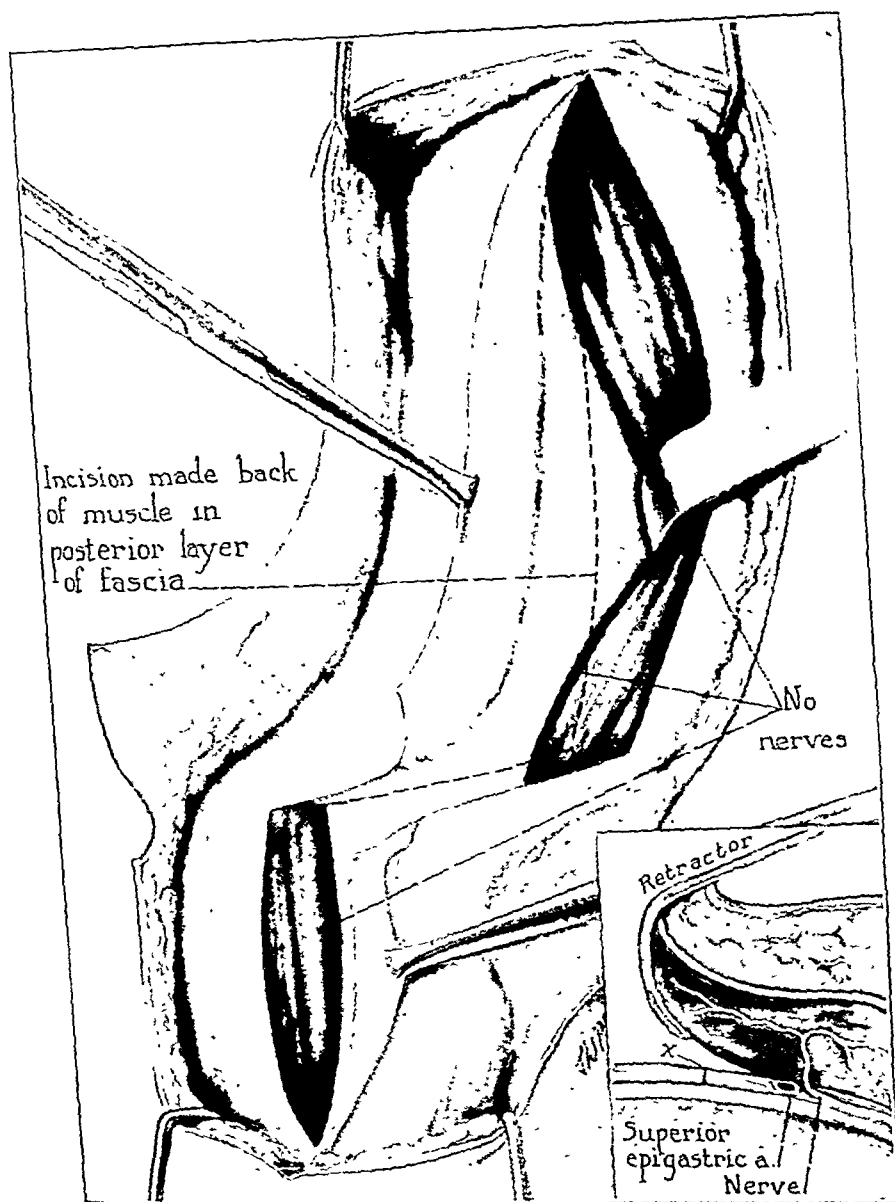


Fig. 4.—The anterior sheath of the rectus muscle is severed to just above the umbilicus, and the left rectus is retracted to the outer side. The diagnosis is made through this upper incision when the operator decides if the incision should be extended to a transverse and right rectus. The dotted line indicates the complete incision. In the insert, a section is shown with the muscle retracted. X indicates the position of the incision through the posterior sheath.

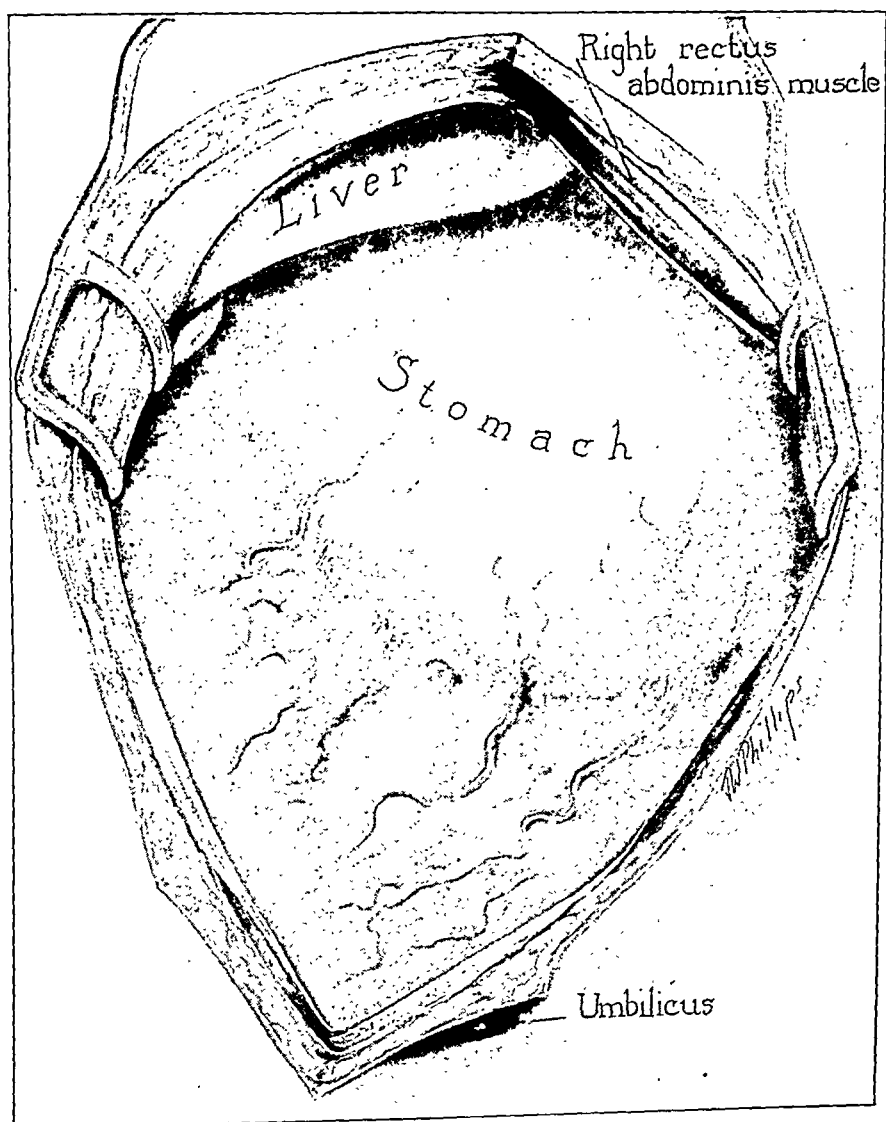


Fig. 5.—Demonstration of the exposure obtained.

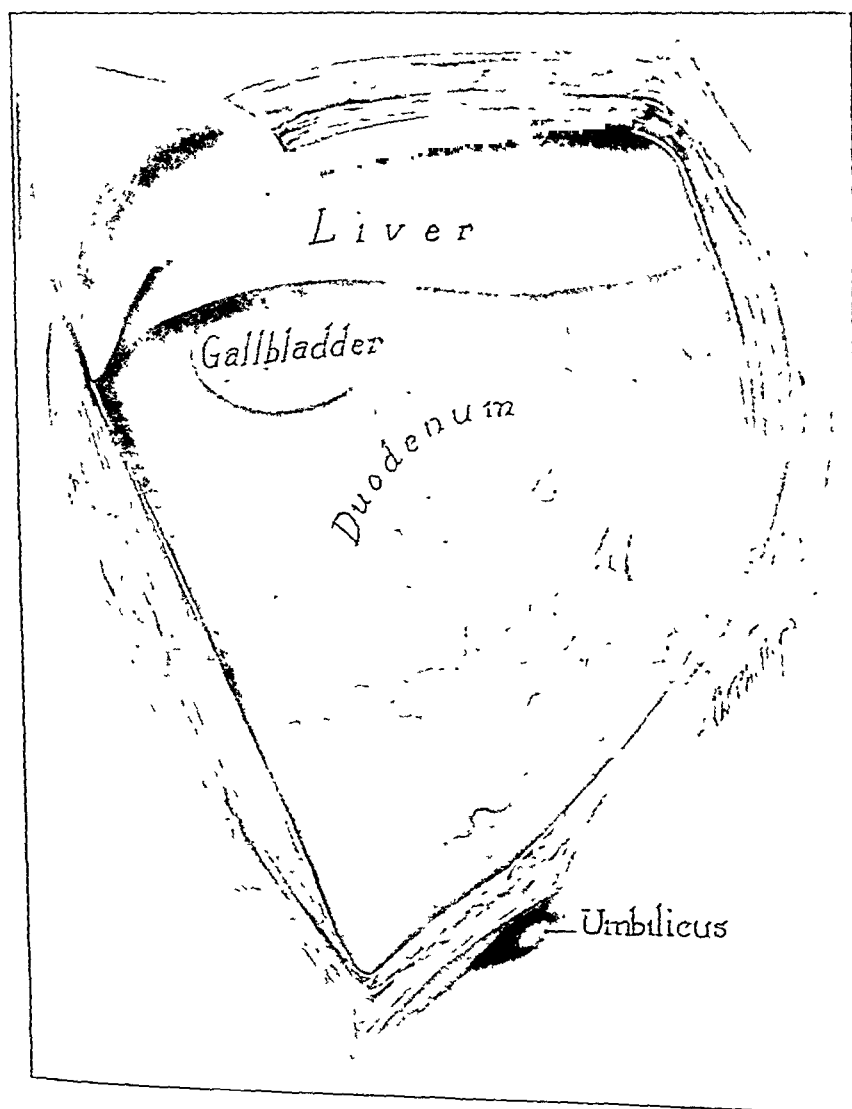


Fig. 6.—Demonstration of the exposure obtained.

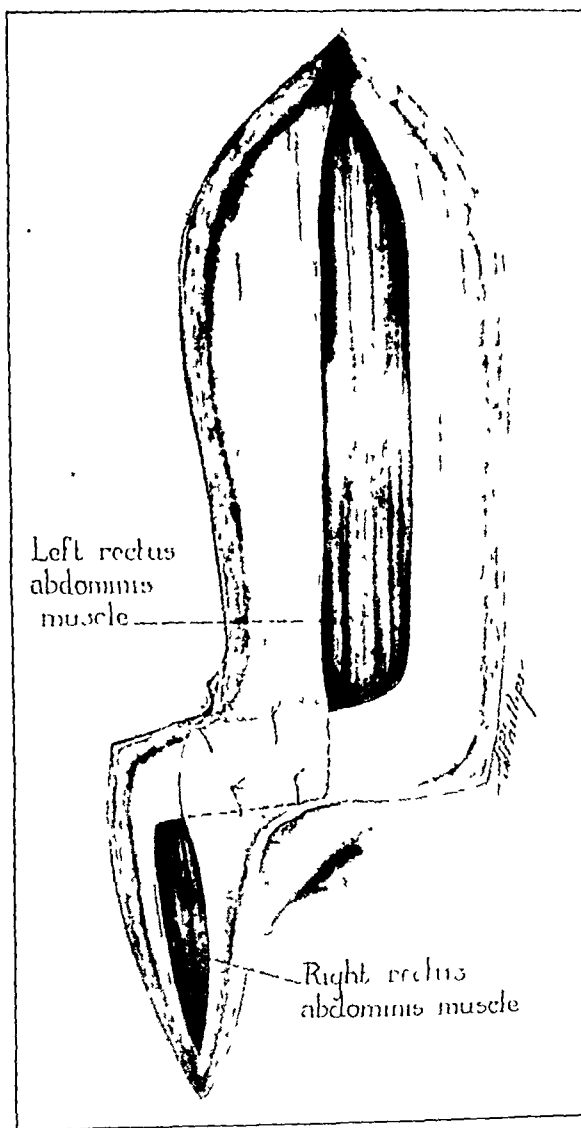


Figure 7

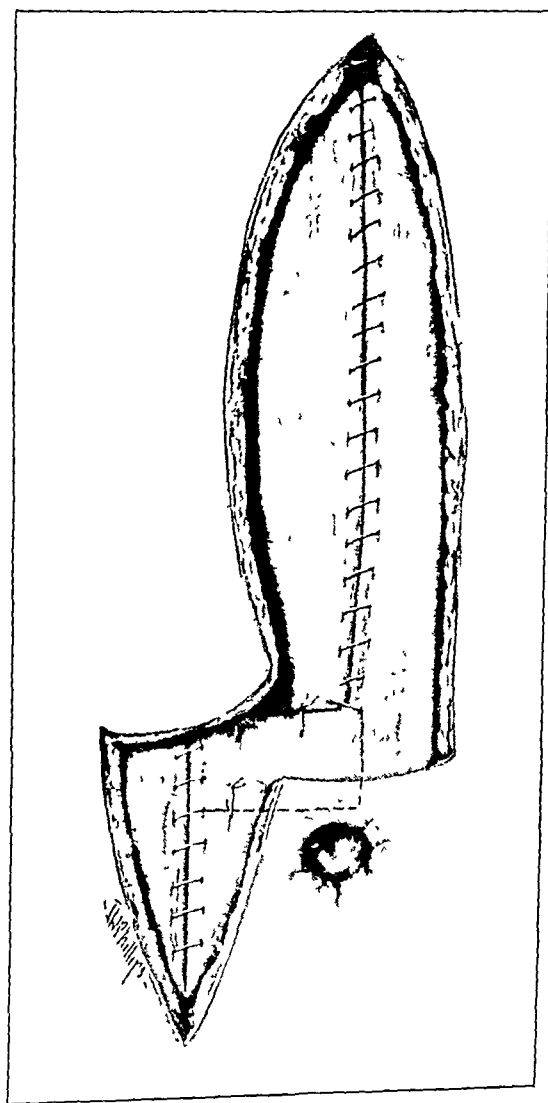


Figure 8

Fig. 7.—First step in the closure. The transverse portion of the incision is imbricated after the manner of the Mayo operation for umbilical hernia. Following the imbrication, the peritoneum is closed with a running suture above and below the transverse incisions.

Fig. 8.—The muscles are allowed to fall back in their accustomed places within the sheath, and the sheath is closed with a running suture of chromic, no 2

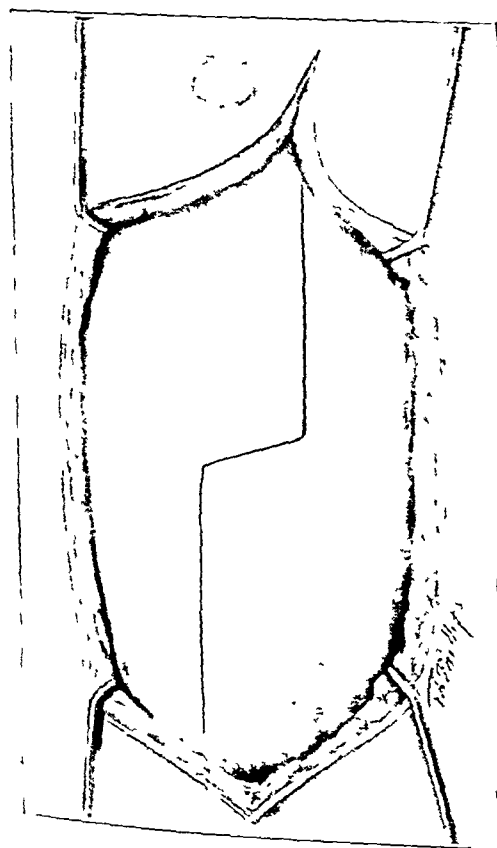


Figure 9

Fig. 9.—The same type of incision is used to prevent hernia in the lower part of the abdomen. One half of the incision is made through the fascia over the left rectus and one-half over the right.

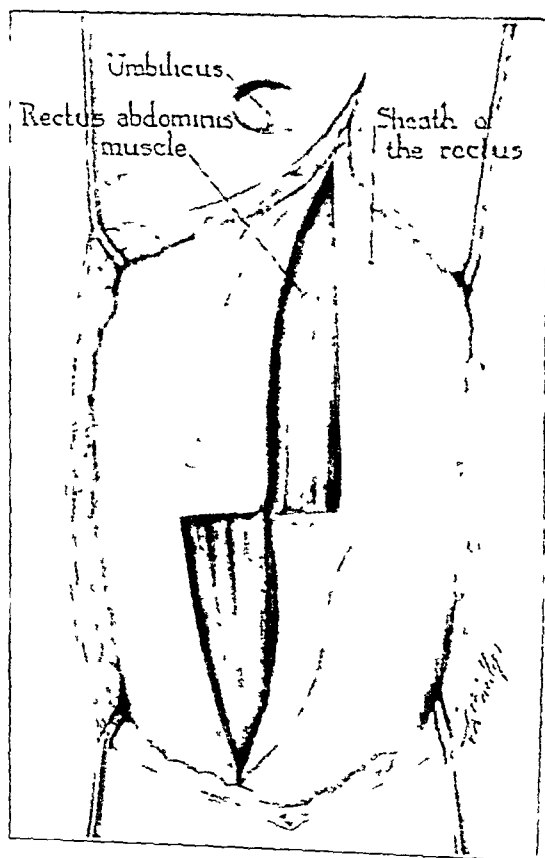


Figure 10

Fig. 10.—The fascia is turned back, showing the right and left rectus muscles exposed.

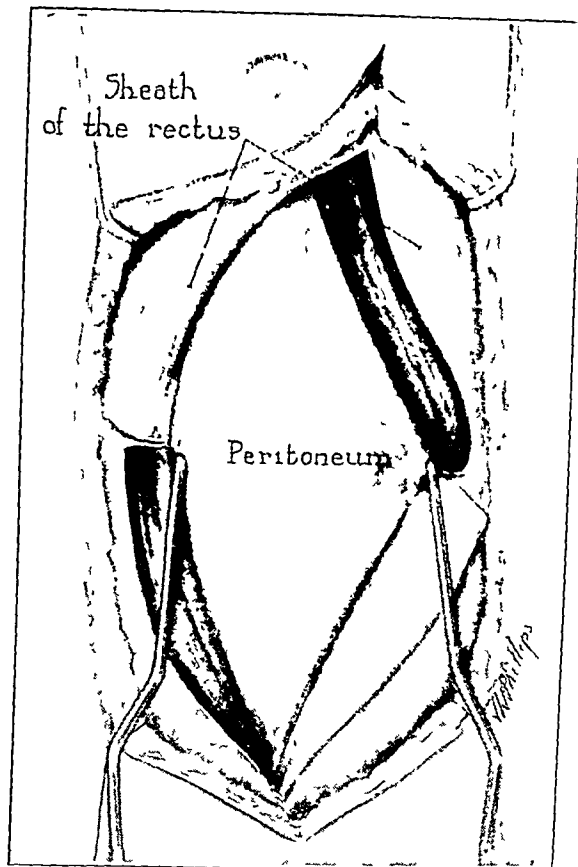


Figure 11

Fig. 11.—The muscle is separated. The left rectus emerges from the sheath above, and the right rectus from the lower sheath.

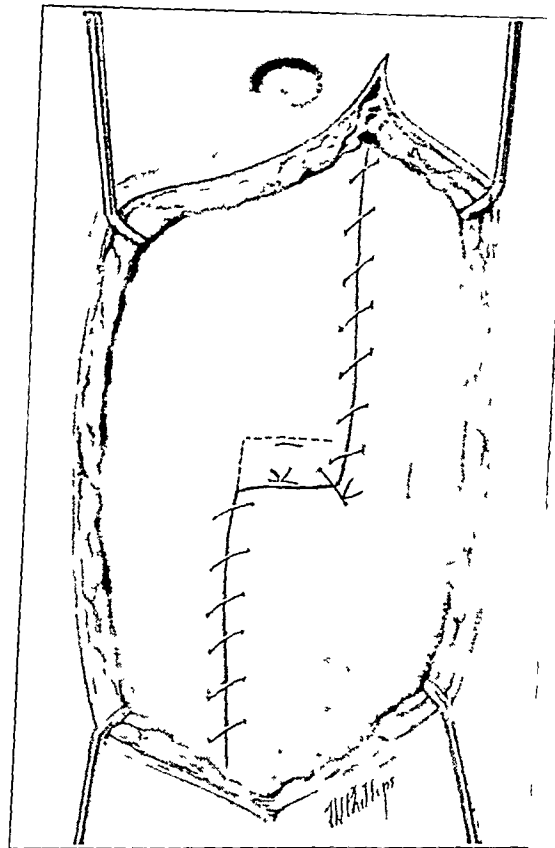


Figure 12

Fig. 12.—The closure is the same as in the upper abdominal' incision. The fascia of the transverse portion of the incision is imbricated from 1 to 2 cm.

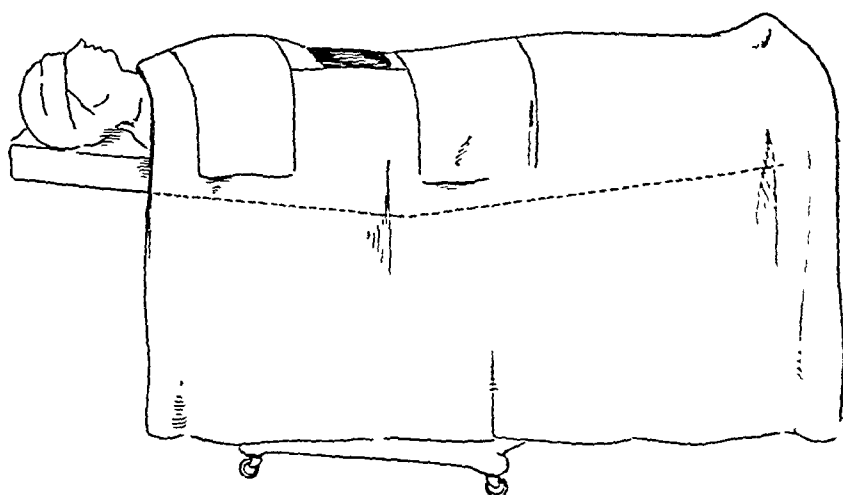


Fig. 13.—When the closure is begun, the patient is flexed on the table, which lessens the tension on the wound.

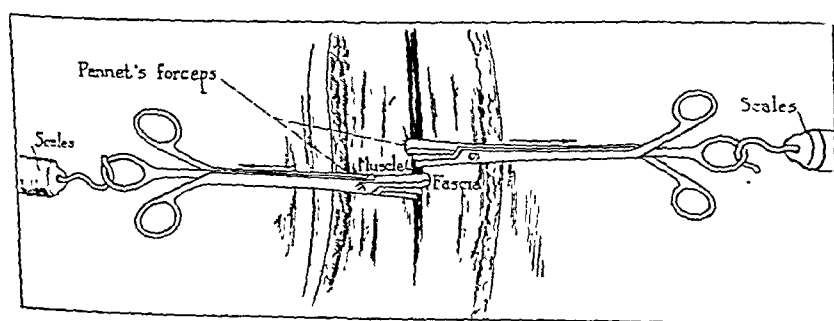


Fig. 14.—The manner in which the lateral tension of the wound can be approximated with forceps and scales.

instead of on one. The strain of abdominal pressure is exerted on the scar in three different places, practically as if there had been three incisions. I have designated the incision as a "three in one incision" because while the abdomen is open it is really one continuous incision, but after closure the effect is that of three distinct suture lines. I believe that this incision lessens the number of postoperative hernias, because after closure the effect is that of three short incisions. As mentioned it has been shown that "the shorter the incision the fewer the hernias." Also, only a few twigs of nerves need be severed and no muscle fibers are cut.

OPERATIVE RELIEF FROM PAIN IN LESIONS OF THE MOUTH, TONGUE AND THROAT*

WALTER E. DANDY, M.D.

BALTIMORE

The recent development of an operative attack on the trigeminal and glossopharyngeal nerves at the brain stem for the cure of trigeminal and glossopharyngeal tic douloureux¹ at once suggested the permanent relief from pain in which the peripheral distribution of both of these nerves are responsible, namely, in chronic ulcers, burns from radium or malignant lesions of the tongue and throat.

The exact form of treatment by which relief from pain is to be sought will necessarily depend on the character, location and rate of growth of the lesion and the general state of the patient's health. At times morphine or other strong sedatives may be the treatment of choice. For the relief from pain confined to the inferior or superior maxillary nerves an injection of alcohol into the peripheral branch may be indicated. Obviously, the operative relief from pain is intended only for a selected group of patients whose general condition and expectancy of life is such as to make it seem advisable.

Since the tongue and pharynx are supplied by two sensory nerves, the glossopharyngeal and the trigeminus, chronic lesions frequently overlap from the domain of one nerve into the other. Under such conditions, the exclusion of only one nerve will have little effect on the intensity of the pain. Both nerves must be divided to give relief.

The trigeminal nerve supplies all of the inner side of the mouth, most of the roof and the floor of the mouth, the anterior two thirds of the tongue and the nasal sinuses. The glossopharyngeal nerve supplies sensation to the posterior third of the tongue, the uvula and the posterior part of the soft palate, the posterior wall of the pharynx and the posterior surface of the epiglottis. Pain is always greatly intensified in ulcerations of the mouth and pharynx because of the passage of liquids and food over the exposed nerve endings. The pain may also be much increased by applications of radium.

The proposal, therefore, for the relief from pain (in selected cases) when the sensory fibers of both nerves are involved or will later probably be involved is the intracranial division of both the fifth and the ninth nerves. Since the intracranial positions of the trigeminal and

* From the Johns Hopkins Hospital and University.

1. Dandy, W. E.: Section of the Sensory Root of the Trigeminal Nerve at the Pons.—Preliminary Report of the Operative Procedure, *Bull. Johns Hopkins Hosp.* 36:2, 1925; Glossopharyngeal Neuralgia (Tic Douloureux), *Arch. Surg.* 15:198 (Aug.) 1927.

glossopharyngeal nerves are in such close proximity, precisely the same approach (subcerebellar) has been used in each procedure. It is possible to divide both nerves at the brain stem almost as easily as either. The sensory root of the trigeminal nerve can be severed with much greater ease and with far less time by this new procedure, which has been used exclusively for the past two years at the Johns Hopkins Hospital and University, than by the older approach along the floor of the temporal fossa (Hartley-Krause). After a small unilateral bony defect has been made, only a few minutes are required to divide the sensory root of the fifth nerve either entirely or in part, and only a few additional seconds are needed to resect the glossopharyngeal trunk. Other great advantages of this route for section of the trigeminus are (1) the constant absence of injury of the motor branch of this nerve and (2) the almost complete absence of corneal redness and ulceration—the two principal deterrent features of the Hartley-Krause method. (3) For reasons not yet definitely ascertained, some sensation to the face is usually but not always retained.

REPORT OF A CASE

A *sallow, undernourished man, aged 40, was suffering terrific pain in the region of an old ulcer on the right side of the tongue; the pain radiated to the back of the throat, the right ear, the lips and teeth on the right side, the inside of the cheek and the right half of the hard palate. The pain was present almost constantly, and though always severe, the intensity varied from time to time. Exacerbations of the pains always resulted from rubbing the mustache and shaving or lightly rubbing the lower part of the face on the right side. The inside of his mouth burned like fire on the right side. Chewing and swallowing so greatly increased the pain in the mouth and ear that he was afraid to eat or drink. The pain was not relieved by any sedative. It was finally necessary to resort to morphine, and many strong doses were required to bring relief. During the three weeks before operative relief was obtained, it had been necessary to give 130 doses of morphine. The patient became desperate and belligerent until the large amounts of morphine reduced the pain to a point of toleration. Most of the right half of the tongue had been removed several months previously for a chronic ulcer, presumably carcinomatous. A few weeks later, the glands of the neck were removed on the right side. Microscopic sections, however, failed to show carcinoma, either in the ulcer of the tongue or in the glands of the neck. Since the ulcer followed in the wake of a healing Vincent's angina, it is more probable that the original ulcer was benign. Six weeks after the operation on the tongue, radium needles were implanted, and thereafter the pain became violent and unrelenting. On the lateral border of the tongue was a contracture due to the healed lesion. It was covered with epithelium and was not indurated. Actual ulceration was not now visible.*

Operation.—Sept. 18, 1927: A unilateral cerebellar exposure was made on the right side. The bony defect extended to the mastoid cells, which, however, were carefully avoided. The cisterna magna was punctured, releasing a large amount of fluid and thereby affording ample room for a subcerebellar exposure. The cerebellum was lifted with a spatula until the cisterna lateralis was brought into view. After evacuation of the fluid of the lateral cistern, one could at once

see the series of cranial nerves on this side. The ninth and the fifth nerves were easily isolated and divided, the former with scissors, the latter with a tiny knife at right angles to a long flexible shaft. The division of both nerves after their exposure probably did not consume more than five minutes, the entire operation taking about forty minutes.

The postoperative course was uneventful. The patient was immediately relieved from all pain, and despite the large doses of morphine which had been given before operation, there has been no further need or desire for the drug. His color, general appearance, weight and behavior rapidly improved. At the time this report was written (Feb. 1, 1928) the patient was back at work and in perfect health. He has gained 30 pounds (30.6 Kg.) in weight, and has been entirely free from all pain since the operation.

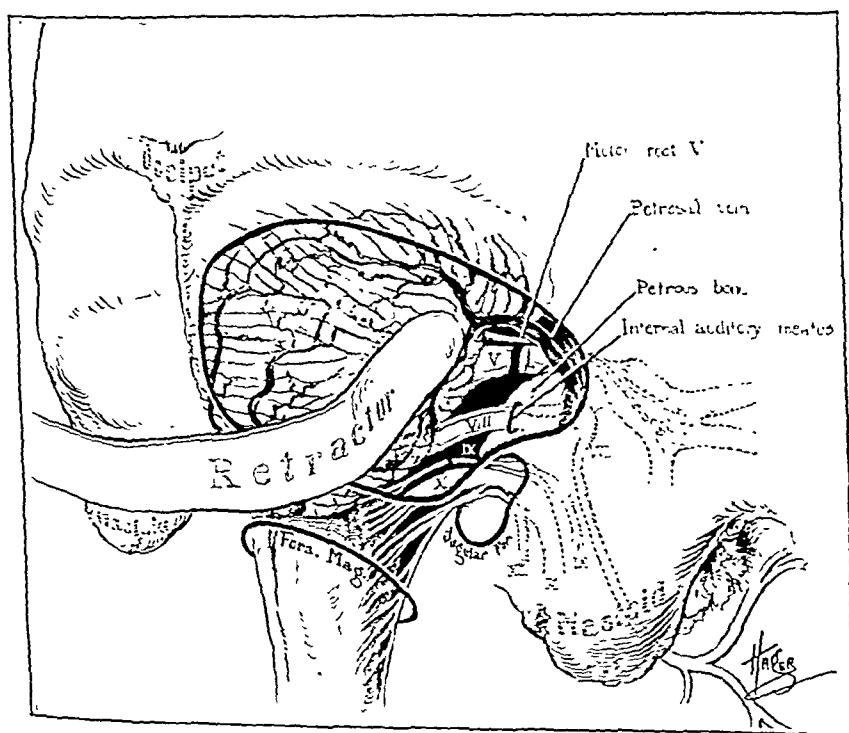


Fig. 1.—Operative approach to the fifth and the ninth nerves at the brain stem.

AFTER-EFFECTS OF OPERATION

The after-effects of the operation are confined to the loss of sensation incident to the loss of the two sensory nerves. However, in not one of three patients in whom the glossopharyngeal nerve alone was divided has there been any appreciation of this sensory loss, nor has the loss of taste over the posterior third of the tongue been noticed, although the objective sensory loss was absolute. Loss of sensation over the trigeminal area is only partial as obtained in seven of ten cases after division of the sensory root at the pons. The sensation over the forehead is only a little impaired; that over the second branch is somewhat more affected, and over the third branch, the loss is a little more.

Touch is preserved over all branches, but most acutely over the first branch. Heat and cold can be differentiated over all branches, but most keenly over the first branch. The corneal reflex is retained. This seeming paradox, i. e., preservation of sensation, is the usual story and greatly reduces the subjective feeling of great numbness which obtained after the old operation. It is not due to partial severance of the nerve as might be suspected. Perhaps there are sensory fibers accompanying the motor branch of the nerve which is always preserved intact.

INDICATIONS FOR AND ADVANTAGES OF THE OPERATION

When the sensory domain of the glossopharyngeal nerve is invaded by carcinoma or a chronic or incurable lesion, relief can be obtained only through section of the ninth nerve.² Alcoholic injections of the



Fig. 2.—Scar of patient whose fifth and ninth nerves were divided intracranially. The photograph was taken ten days after operation.

nerve are practically precluded because of the intimate relations between the peripheral fibers of the vagus, and also because of the fact that the glossopharyngeal nerve lies in the sheath of the jugular vein and close to the internal carotid artery. Peripheral section of the glossopharyngeal nerve in the neck is much more dangerous than intracranial section of the nerve because of the intimate association with the vagus nerve,

2. T. Fay recently divided the ninth nerve intracranially and the upper three spinal sensory roots by a combined laminectomy and cerebellar exposure. He thought it necessary to divide this group of nerves because the more distant skin areas of the neck had been invaded by an ulcerating carcinoma which was primary in the neck (*Intracranial Division of the Glossopharyngeal Nerve Combined with Cervical Rhizotomy for Pain in Inoperable Carcinoma of the Throat*, *Ann. Surg.* 84:456, 1926.)

injury to which induces profound disturbance of deglutition. The vagus has always been injured when section or avulsion of the glossopharyngeal nerve has been attempted in the neck. Moreover, intracranial section of the central fibers of the ninth nerve makes their regrowth impossible, whereas after peripheral division, the pain would doubtless return. Intracranial section is easier and almost devoid of danger.

Should the domain of the trigeminal nerve alone be involved, and the involvement be only on one side, the relief from pain offers the choice of two methods, (1) injection of alcohol and (2) intracranial section (either partial or total) of the sensory root of the trigeminus. If the lesion is a carcinoma and so rapid in its growth that the duration of life is probably a matter of few months, the injection of alcohol into the inferior or superior maxillary branches of the trigeminus would be preferable.

However, should the probable duration of life be many months or years, or should the lesion be such that the duration of life is not directly affected, division of the trigeminal nerve intracranially by the cerebellar route is far superior to the repeated and painful injections with the added loss of the muscles of mastication.

But when with the same expectancy of life the lesion is such that the sensory domains of both the ninth and the fifth nerves are involved, injections of alcohol will be futile. Intracranial section of the ninth nerve alone will give relief in its distribution; and, as previously noted, when this is done the sensory branch of the fifth nerve is already in view and can be easily divided. It need not be emphasized that when the sensory root of the fifth nerve is divided through the temporal route (Hartley-Krause operation) it is not possible to section the glossopharyngeal nerve at the same time, for it is far afield of this exposure. Moreover, there is far less hesitancy in advising division of the sensory branch of the trigeminal nerve by the cerebellar route than by the temporal approach since trophic disturbances of the eye are eliminated and injury to the motor branch of the trigeminal nerve (muscles of mastication) never occurs; finally, the operation has not been attended with mortality.

There remain the possibilities of relieving pain when the lesion is in the midline of the tongue, mouth or pharynx, and involves the sensory fibers of both trigeminal, or of both ninth, or even perhaps of all four nerves. The cerebellar approach to the intracranial part of these nerves is easily extended to a bilateral exposure by enlarging the unilateral into the bilateral approach which is more or less routine in operations for cerebellar tumors. Whether both glossopharyngeal and both trigeminal nerves could be sacrificed, one can only infer. In a case of bilateral trigeminal neuralgia, the sensory roots of both trigeminal nerves have

been divided by this approach at one sitting and with no added operative difficulties other than the greater time consumed in making a bilateral instead of a unilateral cerebellar exposure. The additional division of both ninth nerves, while not difficult technically, might well be impracticable because of the loss of the gag reflex.

Whether chronic lesions of the tongue or nasopharynx would ever present the need of such operative relief, I am not prepared to say. In such cases, bilateral alcoholic injections of the inferior maxillary nerve would be precluded because both motor branches of the trigeminus would be paralyzed and swallowing made impossible. Relief from such pain could hardly be obtained safely except by section of the sensory roots at the pons where the motor roots are safely removed.

Whether both glossopharyngeal nerves could be divided for the relief from pain cannot be answered by precedent. Though technically easy and safe, the absence of the gag reflex on both sides would probably make it impractical. Division of either the ninth or the fifth nerve, or of both on one side, may also be of advantage in permitting the application of radium to a malignant lesion without pain, immediately or subsequently.

SUMMARY AND CONCLUSIONS

An operation is presented for the complete and permanent relief from pain associated with chronic, benign and malignant lesions of the mouth, nose, tongue and throat. When the pain is referable to the sensory domain of both the glossopharyngeal and trigeminal nerves on one side, there is no other way of permanent relief. Under such conditions the glossopharyngeal nerve and the sensory root of the trigeminus can be divided at the brain stem (subcerebellar approach), both nerves being exposed simultaneously in the same operative field. Both nerves can be divided easily, quickly and with little danger to life or function.

NOTE: Since this article was sent for publication, three additional cases of combined fifth and ninth nerve divisions have been performed. In two of the patients the upper three cervical sensory roots have also been divided intradurally because the malignant lesions had extended into the domain of the cervical nerves.

BRONCHOBILIARY FISTULA *

M. G. SEELIG, M.D.

AND

J. J. SINGER, M.D.

ST. LOUIS

During September, 1927, we saw a patient in whom a bronchobiliary fistula developed. The infrequency of this type of lesion prompted us to collect and analyze the literature on bronchobiliary fistulas. We had just instituted our studies when the admirable article by Morton and Phillips¹ appeared, making it not only unnecessary but even unwise to publish another detailed report. In the paper by Morton and Phillips will be found everything pertaining to the history, etiology, pathologic characteristics, symptomatology, prognosis and treatment of bronchobiliary fistula. However, it may be worth while, in a condition so unusual, to submit a report of the case of our patient merely as a matter of record.

REPORT OF A CASE

L. R., an obese, white, married multipara, aged 39, was operated on for appendicitis by one of our colleagues in St. Louis, in the hope of relieving headache, constipation, nausea and pain in the lower right quadrant. The appendix was found to be inoffensive, and exploration of the abdomen yielded no positive information. She was discharged on Sept. 27, 1921, feeling very well. Six weeks later, pain developed in the upper right quadrant, radiating to the back, and was accompanied by nausea and vomiting; the pain occurred in attacks, but was unaccompanied by jaundice or febrile symptoms. Her surgeon decided that the symptoms warranted a direct exposure of the gallbladder. The gallbladder, containing three stones, was small, and bound down to the liver and the duodenum so firmly that it was removed with much technical difficulty. The cystic duct was clamped, and the clamp was left in situ for several days. Six days after the operation, a biliary fistula established itself, and when the patient was discharged from the hospital, eight weeks after operation (April 12, 1924), there was a free discharge of bile from an abdominal fistula in the operative scar.

Six months later, the patient was readmitted to the hospital, complaining of prostration, nausea without vomiting, universal pruritus and persistent diarrhea. She was deeply jaundiced, the stools were clay-colored, showing no trace of bile, and the biliary fistula discharged profusely. At that time, pain was a negligible factor. Her surgeon, suspecting that he had overlooked a stone of the common duct, attempted to locate and remove it; however, owing to dense adhesions and the poor physical condition of the patient, he was unable to locate the duct. After this operation, the patient was seen by Dr. Evarts Graham, who expressed the opinion that there was an obstruction of the common duct, the nature of which

* Submitted for publication, Feb. 2, 1929.

¹ From the Chest and Surgical Services of the Jewish Hospital, St. Louis.

1. Morton, J. J., and Phillips, E. W.: Bronchobiliary Fistula, Arch. Surg. 16:697 (March) 1928.

was not entirely clear, but which was probably the result of an injury to the duct at the time of the former operation, with resultant stricture, and that another surgical attempt should be made to relieve her.

We concurred fully in the opinion of Graham, and on Nov. 25, 1925, an operation was performed. This operation, which was technically difficult owing to the obliteration of all landmarks due to dense adhesion and the absence of the gallbladder, disclosed that the lower portion of the common duct was missing. Between the stump of the duct and the duodenum there was a gap of $1\frac{1}{2}$ inches (3.77 cm.). The duodenum was mobilized, and a small catheter was fixed in the end of the common duct which led into the lumen of the duodenum through a puncture of its superior wall; the duodenum and common duct were then approximated so that they just touched. Sutures held these two structures in loose apposition, and omentum was wrapped around the site of the anastomosis. Following the operation, the stools became colored, the discharge of bile through the fistula ceased, the jaundice cleared up and the patient rapidly returned to a normal condition. The catheter was passed by rectum on the twenty-fourth postoperative day, and the patient left the hospital in excellent condition a month after the operation.

Ten months later, on Sept. 24, 1927, the patient was readmitted to the hospital. She said that she had not felt normal since the last operation; however, she was able to do her work and was not compromised by any definite symptoms pointing to the biliary tract until eight months after operation, at which time she had an attack of nausea and vomiting which lasted three days. Jaundice was not present, though she was almost constantly plagued by pruritus. She did not consult a physician, in spite of the fact that the attacks of nausea and vomiting were repeated at frequent intervals. Finally, after a month of the illness and three days before admission to the hospital, she had a violent attack of pain in the right upper quadrant.

Symptoms and signs at that time were as follows: deep jaundice, yellow sclerae; pale gray stools; highly colored (bile) urine; constant and severe general pruritus with dermatitis from scratching (till blood flowed); acute pain in the region of the liver referred to the back and right shoulder; nausea and vomiting; a temperature of 102 or 103 F., and chills. Physical examination disclosed evidence of compression of the lower lobe of the right lung. Fluoroscopy and roentgenograms showed a high fixed diaphragm on the right side, a normal upper lobe of the right lung with a compensatory air content in the left lung. The white blood count ranged from 13,000 to 22,000.

The history and the previous operations, symptoms and physical signs all pointed to an obstruction of the bile passages complicated by subphrenic abscess or pneumonia of the lower lobe of the right lung. An exploratory operation was decided on, but the condition of the patient was grave, and it was decided to wait a few days. On September 27, definite bronchial breathing with increasing dulness in the lower lobe of the right lung indicated pneumonia. Under these circumstances, operation was postponed. When a roentgen examination was made at that time, we found evidence of a dense shadow in the lower lobe of the right lung extending up to the fourth rib anteriorly. A diagnostic pleural puncture was made, but no fluid was found.

The usual expectant treatment for pneumonia was instituted. On September 30, the patient coughed up lemon-colored sputum which had a bitter taste. The Gmelin test showed the presence of bile. For the next few days, the patient raised considerable purulent sputum heavily stained with bile. The jaundice cleared rapidly with the discharge of the bile through the bronchobiliary fistula

On Oct. 5, 1927, an attempt was made to outline the bronchobiliary fistula by the introduction of iodized oil into the bronchial tree. Unfortunately, we were unsuccessful in this procedure. The patient improved gradually, and the signs of the pneumonic condition of the lobe of the right lung diminished. The patient was discharged from the hospital on October 22, much improved. At the time of writing, one year later, she showed recurrent attacks of jaundice, but neither pain nor cough.

COMMENT

Bronchobiliary fistula is unusual, and in this case was not considered a possibility until bile appeared in the sputum. At the time of the illness (Sept. 9, 1927), it was thought that the fever, chills and signs of septic pneumonia were secondary to a subphrenic accumulation of bile and pus. One occasionally sees bile leakage accumulate either in the subphrenic space or in a dead space about the cystic duct. This fluid frequently gives rise to considerable pain and to jaundice until the pocket is opened. It is most probable that the dilatation of intrahepatic biliary passages occurred, with secondary inflammation, leading to abscess formation and perforation into the subphrenic space. Later, the subphrenic abscess perforated the diaphragm, establishing a bimuicous fistula between the bronchial tree and the intrahepatic bile capillaries and ducts through the intermediate agency of a suppurative pneumonitis. Prompt relief from symptoms followed the expulsion of bile and pus through the bronchial tree. It would have been instructive to have obtained a picture of the two connecting cavities of lung and liver with iodized oil, but the attempt to introduce the oil through the lung was unsuccessful. A study of the literature shows that this procedure was attempted by Oltiker,² with negative results. A study of the roentgenograms showed clearly the pulmonary lesion at the time of the acute symptoms and the clearing up of the pneumonic shadow after the bile was expelled.

2. Oltiker, quoted by Morton and Phillips (footnote 1, page 737).

ENDOMETRIOMA OF THE TERMINAL ILEUM, APPENDIX AND CECUM *

F. N. G. STARR, C.B.E., M.B.

TORONTO

Since Sampson's¹ exhaustive article on perforative hemorrhagic (chocolate) cysts of the ovary, one finds from time to time many and varied evidences of endometriosis. I have seen several such cases² in which the appearance of the uterus closely resembles a leiomyoma, but in which there are many firm dense adhesions to the ovaries, pelvic wall, rectum and sigmoid. In these cases, when trying to arrive at a definite diagnosis, there has always been one definite symptom of which all the patients have complained, pain in the rectum preceding and often accompanying defecation.

The case I shall describe is, I think, unique in that there has never been any menstrual disturbance, and the patient has always been considered a strong, healthy member of her sex.

REPORT OF A CASE

Dr. Donald MacGillivray asked me to see a maiden lady, aged 38, on the evening of March 16, 1927. The history was that for several days she had experienced some discomfort in the right side of the abdomen, which had become more pronounced during the previous night. There had been some constipation, and associated with this there was some nausea but no vomiting. On examination tenderness was found in the right iliac fossa, a comparative rigidity only, but at times a mass could be felt. When this was palpated, a peristaltic wave was observed to extend to the mass. There was evidence of free fluid in the peritoneal cavity. I took this to mean a slowly leaking appendicitis, around which omentum had become lapped, and as the inflammatory reaction increased a partial obstruction had developed. The leukocyte count was 14,000.

When the abdomen was opened, a considerable amount of turbid serum was evacuated. When the cecum was brought into the wound, accompanied by the terminal ileum, no appendix could be seen, nor was there any omentum around the mass. A careful inspection was made to ascertain if the appendix was buried in the posterior wall of the cecum, but none could be found. Because of the almost complete obstruction, a resection was decided on. The terminal ileum about 6 inches (15.24 cm.) from the ileocecal valve, the cecum and part of the ascending colon were removed, and an end-to-end anastomosis was done over the rubber tube.³ The convalescence was uneventful, the tube being passed per rectum on the seventh day. The patient has continued in perfect health.

* Submitted for publication, Feb. 11, 1929.

1. Sampson, J. A.: Perforating Hemorrhagic (Chocolate) Cysts of the Ovary: Their Importance and Especially Their Relation to Pelvic Adenomas of the Endometrial Type, Arch. Surg. **3**:245 (Sept.) 1921.

2. Shirer, J. W.: Canad. M. A. J. **18**:151 (Feb.) 1928.

3. Starr, F. N. G.: Tr. Am. Surg. Soc. **40**:260, 1922.

The pathologist, Dr. W. L. Robinson, reported as follows: The gross specimen consisted of a portion of bowel, measuring 15.5 cm. in length. Its lumen was narrowed by a thickening which involved about two thirds of the circumference of the bowel for a distance of about 2.5 cm. at its longitudinal axis. On one side of the constriction, the wall of the bowel showed a greater circumference than that on the other side. The thickening caused a partial obstruction of the bowel. The lumen barely admitted the finger tip. The cut surface of the bowel was an opaque creamy white and was fibrous. Its margin was indistinct. On microscopic examination, the thickened wall of the bowel was seen. The muscle fibers were hypertrophied, and the fibrous connective tissue of the subserosa was increased in amount. The subserous and the muscle coat, almost up to the mucosa, were invaded by glands typical of endometrium along with stroma precisely like that of endometrium. Some of the glands were large and contained red blood cells and epithelial cells with hemosiderin. There was no inflammatory infiltration and no evidence of malignancy. The appendix as such was not recognized, probably being drawn up into the fibrous tumor mass.

The diagnosis was endometriosis.

The extraordinary feature of this case is that apparently the uterus and adnexa were normal and there was no sign of a chocolate cyst of the ovary. The inference, of course, is that at some time the appendix had been in contact with the fimbria and thus some endometrial cells had come in contact. Possibly it may have become adherent and as the obstruction increased and peristalsis became more vigorous, it was detached, although there was no sign of a recent adhesion on the part removed; however, her first discomfort a few days previously may have been caused in this way.

THIRTY-EIGHTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY

PHILIP D. WILSON, M.D.

LLOYD T. BROWN, M.D.

M. N. SMITH-PETERSEN, M.D.

RALPH GHIORMLEY, M.D.

JOHN KUHN, M.D.

AND

EDWARD CAVE, M.D.

BOSTON

MURRAY S. DANFORTH, M.D.

PROVIDENCE, R. I.

C. HERMAN BUCHOLZ, M.D.

HALLE, GERMANY

GEORGE PERKINS

LONDON, ENGLAND

AND

ARTHUR VAN DESSEL, M.D.

LOUVAIN, BELGIUM

(Concluded from page 2416)

MISCELLANEOUS

The Adult Cripple.—O'Reilly,⁴⁹ in his chairman's address before the Section on Orthopedic Surgery of the American Medical Association, selected for his theme the problem of the adult cripple, and pointed out the all important rôle of orthopedic surgery in helping him to attain economic independence. He urged all orthopedic surgeons to bend their efforts toward improving the standards of treatment and providing better and increased institutional facilities. In order to secure the greatest degree of vocational rehabilitation, it was necessary to obtain the maximum physical rehabilitation. Not only humanitarian motives but economic principles justified the establishment of adequate hospitals manned by expert staffs devoted to the treatment of the adult cripple.

[ED. NOTE.—We believe that O'Reilly has called attention to one of the greatest needs in caring for the sick. Adequate provision in the way of hospital care has been made for the acutely ill patient, and a good beginning has also been made in providing facilities for the treatment of crippled children. The problem that is as yet almost untouched is that of the adult patient with chronic disease. With proper institutional facilities, the wage earning ability of many of these could be restored,

49. O'Reilly, Archer: *Adult Cripple*, J. A. M. A. **91**:137 (July 21) 1928.

and this would relieve society not only of the burden of their care, but of that of providing for those dependent on them.]

Osteochondritis Dissecans.—Reporting on a study of patients with osteochondritis dissecans, Geyman⁵⁰ pointed out that the condition was found chiefly in young adults, and that the sites most commonly involved were the medial condyle of the femur and the external condyle of the humerus. Of the various theories that have been put forward to explain the origin of the disease, he thought that trauma was the most likely cause.

Wolbach and Allison⁵¹ obtained the entire knee joint of a patient who had osteochondritis dissecans, and were able to make a thorough study not only of the loose fragment, but of the bed from which the fragment came and also of the underlying bone. They found that the fragment had been produced by a fracture into a cystlike cavity that had developed in the underlying bone. That the cystic degeneration found in this specimen accounted for all cases of osteochondritis dissecans was not claimed, but it probably offered an explanation of certain cases.

Damage to Bone Growth Resulting from Exposure to Roentgen Rays.—Beck⁵² made a report of six patients in whom a marked limitation of bone growth was noted after repeated exposure to roentgen rays for the treatment of tuberculosis. The treatment had been given from five to fourteen years previously at a time when roentgen treatment was employed in heavy doses. In one patient, the shortening amounted to 15 cm. The writer was inclined to the view that all of the cells of the epiphyseal region rather than only cells of specialized function were damaged. He based this opinion on the general changes noted in the roentgenograms.

[ED. NOTE.—Beck's observations are important, if correct, but one would wish to be certain that the shortening resulted from the roentgen treatment rather than from the disease process itself.]

Osteomyelitis Due to Monilia.—Connor⁵³ described a case of osteomyelitis which was apparently caused by infection with *Monilia* (a type of yeast organism). The patient was a girl, aged 19, who entered the hospital with several draining sinuses located above the elbow. Later, an abscess developed over the buttock, and was found to connect with a focus of osteomyelitis in the ilium. There was no fever and no leukocytosis. An organism was recovered from the pus which was identified as *Monilia psyllosis*.

50. Geyman, M. J.: *Radiology* 11:315 (Oct.) 1928.

51. Wolbach, S. Burt; and Allison, Nathaniel: *Osteochondritis Dissecans*, *Arch. Surg.* 16:1176 (June) 1928.

52. Beck: *Zentralbl. f. Chir.* 55:2849, 1928.

53. Connor, C. L.: *J. Infect. Dis.* 43:108 (Aug.) 1928.

The Functional Importance of Equalization of the Length of the Legs.—That equalization of the length of the legs when one leg was shorter than the other was of great importance for the functional development of the shorter leg, especially in cases of paralysis and other conditions, was stated by Deutschlaender.⁵⁴ The shorter leg was always weaker and more easily fatigued, and rendered the gait uncertain. Raising the sole of the shoe was never a satisfactory means of solution, because it never increased the locomotor power, although it did improve the equilibrium. The writer preferred to shorten the longer leg; sometimes it was necessary to shorten it in more than one place. He had performed the operation of shortening the bone in seventy patients, and had been entirely satisfied with the results. The operation had resulted in making the legs of almost equal length and in greatly improving the gait. All of the patients were enabled to wear ordinary shoes.

[ED. NOTE.—The question to determine here is whether it is better policy to equalize the length of the legs by shortening the long, or normal leg, or by lengthening the short leg. Until recently, the results of the procedure of lengthening the bone were uncertain, but substantial progress has been made by Abbot in the use of an improved method described in a previous "Report of Progress in Orthopedic Surgery."⁵⁵ As familiarity with this technic is acquired, we believe that it will be preferred to the operation of shortening the bone.]

Spontaneous Dislocation and Destruction of the Tendon of the Biceps Brachii.—From studies of the shoulder joint in cadavers, Meyer⁵⁶ concluded that spontaneous partial or complete forward dislocation of the portion of the biceps tendon lying between the tuberosities of the humerus was not an uncommon occurrence. It probably occurred most frequently in laborers past middle age. Division of the tendon in this portion might occur as the result of degenerative changes and of the process of wear and tear, but usually the tendon reattached itself to the humeral shaft just beyond the lesser tuberosity. If this reattachment did not occur, a marked atrophy of the lateral belly of the biceps muscle resulted.

Traumatic Osteoporosis of the Carpal Bones.—Buchman⁵⁷ discussed osteoporosis of the carpal bones (Kienböck's disease; Preiser's disease) in respect to etiology, pathology and treatment. He believed with Leriche that in this disease there was a disturbance of vasomotor

54. Deutschlaender, K.: Ztschr. f. Orthop. Chir. **51**:64, 1929.

55. Abbott, LeRoy: Reference in Thirty-Fourth Report of Progress in Orthopedic Surgery, Arch. Surg. **16**:620 (Feb.) 1928.

56. Meyer, A. W.: Spontaneous Dislocation and Destruction of Tendon of Long Head of Biceps Brachii, Arch. Surg. **17**:493 (Sept.) 1928.

57. Buchman, Joseph: Ann. Surg. **87**:892 (June) 1928.

equilibrium; that a fracture frequently accompanied, but was not essential to, the process; that absorption began regardless of whether a fracture was present or not, and that fracture and extensive destruction occurred as a result of the atrophy. Conservative treatment in the form of immobilization in the "cock up" position should be tried for a reasonable length of time, but if disability persists, then the involved bones should be excised. In the hands of the author, the operative treatment had given good results.

He reported seven cases; in three, the process involved only the scaphoid; in the fourth the scaphoid and semilunar; in the fifth the scaphoid, semilunar and os magnum; in the sixth the semilunar, os magnum, and unciform, while in the seventh the os magnum and unciform were affected.

[ED. NOTE.—Traumatic osteoporosis is a most baffling condition and sometimes defies all treatment. Its cause is obscure, but the general tendency is to regard it as a trophoneurosis. All surgeons who have had first hand acquaintance with the lesion will welcome any new light that may be shed on it.]

Stenosing Fibrous Tendovaginitis Over the Radial Styloid.—Since de Quervain's original description of stenosing fibrous tendovaginitis over the radial styloid, Schneider⁵⁸ found that 144 cases illustrating the condition had been reported. It was caused by excessively monotonous motions of the thumb in abduction and extension, these leading to a thickening of the tendon sheaths of the abductor pollicis longus and the extensor pollicis brevis as they passed over the radial styloid. It occurred more often in women.

In most of the patients relief was to be obtained by complete immobilization with the thumb in a position of abduction and extension over a period of from six to eight weeks. In a few obstinate cases, it was necessary to expose the seat of the trouble by an incision and to split the tendon sheath.

SURGICAL PROCEDURES ON THE BONES, JOINTS AND TENDONS

Spinal Fusion with Osteoperiosteal Graft.—Allison⁵⁹ described the technic of spinal fusion with the aid of the osteoperiosteal graft which had been employed at the Massachusetts General Hospital for a number of years. The operation consisted essentially of the Hibbs procedure with the addition of a thin osteoperiosteal graft in the shape of a long flexible ribbon which was removed from the anteromedial surface of the tibia and laid down on the surface of bone chips and fragments pro-

⁵⁸ Schneider, Chester C.: Surg. Gynec. Obst. 46:846 (June) 1928.

⁵⁹ Allison, Nathaniel: Surg. Gynec. Obst. 46:826 (June) 1928.

duced by the spinal operation. In the author's opinion, the addition of this osteogenetic material served to stimulate the production of a greater amount of new bone than would otherwise be obtained and hence represented an additional guarantee of a successful outcome. The graft was always removed by a second operating team and hence did not prolong the time of the operation or add to the shock.

Enlargement of Parturient Canal by Bone Graft.—Albee⁶⁰ reported that in two patients with contracted pelves he had successfully enlarged the pelvic outlet to permit childbirth. The technic consisted of inserting at the symphysis pubis a bone graft 1½ inches (3.7 cm.) long which was removed from the tibia.

[ED. NOTE.—While concerning chiefly the sister specialty of obstetrics, this procedure ought to be of much interest to orthopedic surgeons, particularly as it affects the mechanics and function of the sacro-iliac joints.]

Transtrochanteric Approach to the External Iliac Fossa in Osteoplastic Operations.—For certain operations on the hip, such as the shelf operation in congenital dislocations, the procedure of arthrodesis and bone grafting in ununited fractures, Calvé⁶¹ described a new T-shaped incision. The long vertical limb of the incision was made to extend from the base of the lateral surface of the greater trochanter to the iliac crest at the junction of the anterior third with the posterior two-thirds. From the summit of this incision two shorter cross incisions were made, one extending anteriorly and the other posteriorly following the curve of the iliac crest. The deeper tissues were then separated, exposing the greater trochanter but without dividing the muscles attached to the latter. The edges of the gluteus medius and gluteus minimus were then defined and separated. Proceeding carefully at this point, the operator exposed the arterial and venous branches of the gluteal vessels; these branches were then clamped and cut between ligatures. The greater trochanter was next sectioned by a vertical incision extending from its summit for a distance of from 1 to 2 cm., at which point it separated into two oblique incisions, the anterior one running forward and outward, the posterior one running backward and inward. The two fragments of the trochanter were then retracted without being completely separated from their femoral attachments. One thus obtained a wide exposure of the capsule of the joint, the acetabular margin and the external surface of the ilium.

[ED. NOTE: It is difficult to see how injury to the nerve supply of the tensor fasciae femoris muscle could be avoided by this incision.]

60. Albee, F. H.: Surg. Gynec. Obst. **46**:845 (June) 1928.

61. Calvé, Jacques: Presse méd. **36**:695 (June 2) 1928.

Arthroplasty of the Knee.—Campbell⁶² discussed the results of arthroplasty of the knee, basing his remarks on a study of 111 patients. He employed an operation which remodeled the lower end of the femur in the form of a single condyle extending across the transverse diameter of the bone, this articulating with a concavity in the upper surface of the tibia. Fascia was interposed between the ends of the bones. In forty-three of 111 patients whom he was able to follow, a useful range of motion resulted, varying in extent from 35 to 120 degrees. As experience with the operation increased, a betterment of the functional results was noted. The indications, contraindications and postoperative treatment were thoroughly discussed.

Albee⁶³ described how his own conservative attitude of ten years ago concerning arthroplasty for bony ankylosis of the knee had changed to one of moderate enthusiasm because of ten successful results he had obtained by operation since 1920. He analyzed these cases, calling attention to the technical features which had contributed to the favorable outcome. He believed that the technic of wedge-shaped arthroplasty with the reconstructed convex femur fitting into the concave tibia maintained mobility and at the same time prevented lateral instability. For interposition, he employed fascia which was covered with a layer of fat. He did not believe that old healed tuberculosis of the knee was necessarily a contraindication to arthroplasty.

[ED. NOTE.—The increasing number of favorable reports on arthroplasty of the knee shows that in skilled hands the operation here yields better results than in the case of most of the other joints, with the exception of the elbow and the jaw.]

The Operation of Stripping the Os Calcis.—Describing the technic of his operation of stripping the os calcis for pes cavus, Steindler⁶⁴ stated that he always used the medial incision and never the incision around the heel. He emphasized the importance of thoroughly stripping the structures as far forward as the calcaneocuboid joint. In addition to the stripping of the os calcis, wrenching of the foot or some other operation on the bones often was necessary to restore and maintain the balance of the foot. An analysis of the results obtained in 201 patients who had been followed for a number of years was presented.

A Conservative Operation for Bunions.—McBride⁶⁵ described an operation for the correction of hallux valgus which he had employed in a large number of cases. The operation consisted of transplanting the conjoined tendons of the adductor muscle group of the great toe to

62. Campbell, Willis C.: Surg. Gynec. Obst. **47**:89 (July) 1928.

63. Albee, F. H.: Surg. Gynec. Obst. **47**:312 (Sept.) 1928.

64. Steindler, Arthur: Surg. Gynec. Obst. **47**:523 (Oct.) 1928.

65. McBride, Earl: J. Bone & Joint Surg. **10**:735 (Oct.) 1928.

the dorsum of the head of the first metatarsal bone. The bursa was also dissected out and the bony prominence chiseled away. After the capsule was repaired and the wound closed, a light plaster casing was applied. McBride permitted weight bearing at the end of two weeks.

FRACTURES

Fractures in Industry.—From an analysis of the experience with several thousand fractures covering a period of twelve years, Davis⁶⁶ found that it was possible in simple uncomplicated fracture to predict the cost of treatment in the average case fairly accurately. The average period of time lost in this group of cases was 27.3 days. The actual cost to the injured employee was based on the average time lost and the average of the different earnings, and amounted to \$6.00. The actual cost to the employer was \$20.97 a week when the patient was not hospitalized and included the cost of taking care of the fracture plus compensation. When the patients were hospitalized, their sustenance had to be added, and this amounted to \$31.78 a week. When the patients were sent to a private hospital, the cost was much greater and included the minimal ward rate of \$3.50 a day, the laboratory fee and the cost of materials, the professional charge of the physician and compensation to the employee. The figures indicated that the percentage of disability could be reduced by skilful operative procedures and careful postoperative treatment. In many instances the period of disability was prolonged, and the cost both to himself and to his employer was increased by the poor physical condition of the patient.

Bone Repair and the Healing of Fractures.—Cowan⁶⁷ produced simple fractures in the bones of kittens and studied the reparative processes grossly, microscopically and roentgenologically at intervals varying from twelve hours to thirty-four days. He concluded that the periosteum was more essential in healing than the medullary tissue or cortical bone. Fibrous union or pseudarthrosis was more apt to develop following extensive destruction of periosteum at the fracture line or after wide separation of the fragments. If after fibrous union was established, weight bearing was permitted, a false joint often developed at the fracture site. To overcome this, it was necessary to excise the fibrous and cartilaginous tissue.

Mock⁶⁸ was of the same opinion as Cowan and cited clinical and experimental evidence to substantiate his claim that of all the elements of bone, the periosteum was the most important in bone repair. In delayed union or loss of bone substance, he would practically always use

66. Davis, P. A.: *Fractures in Industry*, J. A. M. A. **91**:695 (Sept. 8) 1928.

67. Cowan, John: *Ann. Surg.* **88**:749 (Oct.) 1928.

68. Mock, H. E.: *Surg. Gynec. Obst.* **46**:641 (May) 1928.

the periosteal graft or if the defect were too great he would prefer an osteoperiosteal strip.

In experiments on kittens, Glaessner and Hass⁶⁹ found that thymectomy delayed the formation of callus, and that injection of an extract of thymus hastened bone consolidation. In a series of experiments on older cats, the influence of extracts of various endocrine glands was tested. Thymus extract was found to be the most potent in its effect on formation of callus. The next most potent extract was that of the parathyroids. These authors had employed the extract in a considerable number of patients with delayed callus formation and had noted beneficial results.

Fine and Brown⁷⁰ performed some experiments on dogs to study bone repair under the influence of parathyroid extract-Collip. They concluded that the experiments, although small in number, showed that the parathyroid extract delayed the speed of deposition of calcium in regenerating bone in young dogs, whereas in adult dogs no clear evidence as to its potency in this or in the reverse direction was obtained. In their opinion the practical significance of these observations was that the clinical use of the parathyroid extract for delayed bone union was not based on any sound principle, could do little if any good and, in fact, might do harm.

Robinson⁷¹ made a study of the rôle of the circulation in the healing of fractures and came to the conclusion that an inadequate blood supply was one of the most important factors contributing to delay and failure of bone repair. He emphasized the necessity of an adequate supply of new blood vessels for the deposition of lime salts in the callus. He pointed out the importance of making provision for expansion of the surrounding soft structures in the treatment for fractures, of avoiding compression by tight bandages, and of splitting circular plaster casing on two sides.

Fracture and Dislocation of the Sternum.—Three instances of fracture or dislocation of the sternum were reported by Holderman.⁷² From a statistical review, he found that this type of fracture represented considerably less than 1 per cent of all fractures. It was usually produced by a direct blow, but might also result from indirect violence. The commonest site of separation of fragments was at the junction of the manubrium and gladiolus. In most instances the dislocation could be satisfactorily reduced by closed methods, but open operation was often justified.

69. Glaessner, K., and Hass, I.: *Klin. Wchnschr.* 7:1633 (Aug. 26) 1928.

70. Fine, Jacob; and Brown, Samuel: *New England J. Med.* 198:932 (June 21) 1928.

71. Robinson, Wilton H.: *Rôle in Healing of Fractures*, *Arch. Surg.* 17:420 (Sept.) 1928.

72. Holderman, Herbert: *Ann. Surg.* 88:252 (Aug.) 1928.

Fracture of the Clavicle.—Funston⁷³ described a splint for the treatment of fractures of the clavicle. It was based on the principles of the clavicular cross, but did away with the mechanical objections to it of bulkiness and of pressure against the vessels and nerves in the axilla as well as the loss of tension when the dressings had loosened. The splint was made of steel rods about $\frac{1}{4}$ inch in diameter and was furnished with special pressure drums covered with felt which exerted a strong pressure on the front of the heads of the humeri in a backward direction. Steel rods passed backward from these, arching under the axillae without making any pressure and terminated in two pressure pads pressing against the back in the interscapular region. These were connected with a vertical member of the brace which extended down the back for the purpose of exerting leverage, its end being held in place by a circular strap about the pelvis.

Yates and Guest⁷⁴ recorded an unusual complication of fracture of the clavicle. A woman, aged 41, died of cerebral embolism due to thrombosis of the subclavian artery which had been caused by pressure of an ununited fracture of the clavicle.

[ED. NOTE.—Funston's splint is ingenious and ought to be effective. Unfortunately, the services of an experienced brace fitter and a considerable amount of time are required for its manufacture.]

Vertebral Fractures.—Wilmoth⁷⁵ presented the case histories of seventeen patients who had fractures of the transverse processes or chip fractures of the lumbar vertebrae. He was of the opinion that such injuries were of relatively frequent occurrence and were due to forcible hyperextension of the spine or to sudden muscular action. The trauma was usually slight, and this led to incorrect diagnosis as the injury did not seem sufficient to justify roentgen examination. As far as treatment was concerned, it ought to be the same in chip fractures as in other types of fracture, namely, rest and immobilization.

[ED. NOTE.—The chief feature of interest in this article is the suggestion that hyperextension of the spine may cause a chip fracture of the spine as well as hyperflexion. The observation needs to be confirmed.]

Kümmell's Disease.—In a thorough article reviewing the literature and what is known of the pathology, Cardis, Walker and Oliver⁷⁶ reported fourteen cases of Kümmell's disease. They were able to study the lesion in a patient who died from an intercurrent disease. Examina-

73. Funston, Robert: J. A. M. A. **91**:794 (Sept. 15) 1928.

74. Yates, A. Gurney; and Guest, Denton: Lancet **2**:225 (Aug. 4) 1928.

75. Wilmoth, Clifford L.: Fractures of Lumbar Vertebra Due to Hyperextension and Extreme Muscular Action, J. A. M. A. **91**:6 (July 7) 1928.

76. Cardis, J.; Walker, G. F., and Oliver, R. H.: Brit. J. Surg. **15**:616 (April) 1928.

tion of the specimen showed no signs of injury of the spinal cord, no evidence of tuberculosis or abscess, no bone necrosis and the absence of pathologic changes in the intervertebral disk. The second lumbar vertebra was wedge-shaped. The margins of the bone were intact, except for a small fracture in the upper anterior part. The spongiosa showed multiple small hemorrhages. On microscopic examination the bony framework showed marked atrophy with a changed appearance of the marrow, the cells of which were decreased in number and stained poorly.

Fractures of the Pelvis.—Sever⁷⁷ made a study of fifty-one patients with fractures of the pelvis. He classified these as follows: fractures of the ilium, twelve; fractures of the pubic arch, twenty-five, and fractures involving the acetabulum, fourteen. In fractures of the ilium without lesions of the abdominal contents, treatment gave good results. Acetabular fractures were of two types: first, those which merely showed fissures in the acetabulum as well as those with slightly greater involvement, that is, where there had been a little protrusion of the inner wall or a spicule broken off from the inner table; second, those which showed protrusion of the whole acetabular wall or even a penetration of the femur into the pelvis.

In the first class, good function and little or no disability resulted. In the second class there was always some disability, often considerable, with some limitation of the motions of the hip. Treatment might modify this eventual disability somewhat. The age, occupation and habits of the patient might modify it more. There was the possibility that secondary changes might develop in the course of time and still further affect the function of the joint.

[ED. NOTE.—We have observed marked interference with function after deforming fractures of the acetabulum, especially those in which the femoral head penetrates the acetabulum. We believe that every effort should be made to correct the deformity in the early stage. The method described by Putti of two way skeletal traction would appear to offer an effective remedy.]

Dislocations and Simple Fractures of the Elbow.—Geist and Henry⁷⁸ reviewed 150 consecutive cases of simple fractures and dislocations about the elbow joint. The ages of the patients varied from 4 months to 77 years; 54 per cent of the cases occurred before the age of 16, and 20 per cent occurred between 21 and 30.

Of the dislocations, the posterior variety was the most common, constituting 6 per cent of the injuries. Backward dislocation with fracture occurred in 3.4 per cent of the patients. Internal lateral dislocation was present in 1.4 per cent of the patients. In 2 per cent a dislocation of

77. Sever, James Warren: *New England J. Med.* **199**:16 (July 5) 1928.

78. Geist, E. S., and Henry, M. O.: *Minnesota Med.* **11**:509 (Aug.) 1928.

the head of the radius occurred. There were no cases of anterior or divergent dislocation.

The fractures were divided as follows: the lower end of the humerus, 61.4 per cent; the upper end of the radius, 10.7 per cent; the upper end of the ulna 8.6 per cent; explosion fracture (shattering of all bones), 6 per cent. The ulnar nerve was injured in several of the fractures of the internal condyle. The prognosis was considered serious in fractures of the head and neck of the radius, and it was often necessary to remove the radial head. The authors advised operative suture in all cases of fracture of the olecranon with displacement. They considered the prognosis bad in all patients with shattering fractures of the lower end of the humerus. They obtained better results by conservative treatment than by operative treatment in this type of fracture. They advocated immobilization of the elbow in a position of 75 degrees flexion with early active and passive motion.

Fractures of the Upper End of the Femur.—By experiments performed on the cadaver, Shaw⁷⁹ was able to refute the contentions of Stebbing based on clinical observations that intertrochanteric fractures of the femur were due to indirect violence and that direct violence on the trochanter caused a fracture of the acetabulum, rather than an intertrochanteric fracture. Shaw was able to produce intertrochanteric fractures by the application of direct violence to the trochanter and also by outward leverage on the shaft of the femur when the head and trochanter were fixed. Axial force applied to the femur (hammering on the lower end of the shaft) did not cause an intertrochanteric fracture. He was unable to produce a fracture of the acetabulum, although increasing powerful pressure on both trochanters caused fractures of the rami of the pubis and ischium.

Skeletal Traction in the Treatment of Fractures.—Groves⁸⁰ described his technic for applying skeletal traction in the treatment for fractures. He preferred transfixion pins to nails, ice tongs or Finochietto's stirrup. He transfixed the femur above, not through, the condyles to avoid the synovial sac of the knee joint and to obtain a pull from the dense bone of the shaft rather than from the cancellous bone. For fractures of the lower third of the femur and those involving the knee joint, he transfixed the crest of the tibia just below the tubercle. He employed traction force of from 20 to 60 pounds (9 to 27 Kg.), with counter traction obtained by raising the foot of the bed 12 inches (30.5 cm.) and passing padded perineal bands round each thigh and tying them to the upper posts of the bed. In treating fractures of the tibia and fibula, he transfixed the posterior process of the os calcis as far back as possible in

79. Shaw, J. J. M.: Brit. J. Surg. 16:120 (July) 1928.

80. Groves, E. W. Hey: Brit. J. Surg. 16:149 (July) 1928.

order to counteract the pull of the tendo achillis; in fractures through the upper third of the leg bones or in fractures of the ankle with separation of the tibia and fibula, however, he preferred to transfix the malleoli. He seldom used skeletal traction in the upper limb, although occasionally he found it necessary to transfix the olecranon, using a 10 pound (4.5 Kg.) weight, in severe fractures of the humerus just above or into the elbow joint.

Living Suture Grafts in the Repair of Fractures and Dislocations.—Allen⁸¹ reported that he had employed strips of fascia lata for the suture of fractures of the patellae and olecranon in a series of patients who had been followed over a period of several years. The technic consisted in passing the strip through holes drilled in the fragments, crossing the ends on the anterior surface of the patella by passing one through the other and suturing the ends to the fascia or tendon above and below the fracture. The lateral tears in the aponeuroses were repaired with chromic gut. The advantages of the method were its strong mechanical fixation and the ability to stand the strain of motion begun at the end of one week. Splinting was not required. In the patients followed, there were no refractures and functional recovery was obtained at an earlier period than when the fragments were sutured by the usual methods.

Allen also successfully employed fascia lata for securing dislocations of the sternal end of the clavicle and for fixing the radial head in a patient with recurrent dislocation of this bone.

[ED. NOTE.—Allen developed his method of fascial repair of fractures of the patella and olecranon on the Fracture Service of the Massachusetts General Hospital, and the method has appeared to have so much advantage that it has been generally adopted by the other members of the staff.]

DISLOCATIONS

Fracture Dislocation of the Shoulder.—Gerard-Marchant⁸² made a study of fracture dislocations of the shoulder, including only those cases in which there existed a complete interruption in the continuity of the bone between the head and the upper part of the shaft. His conclusions were based on an analysis of 353 cases.

He found that the anteromedial type of dislocation was almost the rule, and that the fracture involved the surgical neck in 51 and the anatomic neck in 38.5 per cent of the cases. He was unable to note any difference in the type of the articular lesion accompanying the two varieties of fracture.

81. Allen, Arthur: *Living Suture Grafts in Repair of Fractures*, Arch. Surg. 16:1007 (May) 1928.

82. Gerard-Marchant, M. P.: *J. de chir.* 31:695 (May) 1928.

Reviewing the different methods of treatment and their results, he called attention to the fact that reduction might be accomplished in a certain number of patients by closed methods irrespective of whether the fracture involved the surgical or the anatomic necks. Complete functional recovery was obtained in about one half of the patients in whom reduction was accomplished by this means. Of the open methods of treatment, resection—that is, the excision of a larger or smaller entirely detached fragment—when performed soon after the injury, yielded on the whole imperfect results. The results of late resection were better. Replacement of the dislocated fragment by open operation performed soon after the injury gave results superior to those obtained by other methods. Late reductions gave varying results.

Actually, the methods of choice were, first, closed reduction and, second, open replacement. In fractures of the anatomic neck, these two methods appeared to be of about equal value; in fractures of the surgical neck, open replacement seemed to be the better method. Against closed reduction were the dangers of nerve injury or vascular rupture but, on the other hand, opening the articulation by surgical incision was not without danger. The open method ought not to have absolute priority over the closed method except in case of neurovascular lesions. In fractures of the surgical neck, one ought never to resort to resection. In fractures of the anatomic neck, resection might be indicated under certain conditions. In fractures involving the upper end of the humeral shaft, replacement could be the only aim. In the comminuted fractures in which the head escaped from the capsule in fragments, it was necessary to be sparing in the resection of the fragments.

Discussing the treatment for fracture dislocations of the shoulder, Taylor⁸³ described a method of treatment which he had successfully employed in several cases. Instead of manipulating or performing an open operation, he applied traction with the arm in abduction and the patient recumbent. He reported one case in which reduction was effected in four days. The fracture was reduced by increasing the degree of abduction of the arm to 120 degrees. Union was sufficiently solid in three weeks to allow immobilization in a plaster casing.

[ED. NOTE.—Of the various bony injuries, we know of none in which treatment is more difficult or prognosis more uncertain than fracture dislocations of the shoulder. When the fracture involves only the greater tuberosity the problem is relatively simple, and reduction can generally be accomplished by the closed method. Gérard-Marchant's conclusions as to the superiority of open replacement over resection are in accord with our own observations, although the operation is

83. Taylor, R. T.: Fracture Dislocations of Shoulder, *Arch. Surg.* **17**:475 (Sept.) 1928.

attended by much greater difficulty. Even then, complete functional recovery cannot be expected. We shall be interested to try the method described by Taylor. In obese patients, or when for any reason open operation is contraindicated, we think that there is something to be said for the old method of waiting for three to four weeks to allow the fracture to unite before attempting closed reduction.]

Dislocation of the Carpal Semilunar Bone.—Ettorre⁸⁴ preferred the term traumatic enucleation of the semilunar bone to dislocation, pointing out that the cases fell into two classes, one which he called a perilunar luxation in which the displacement was between the semilunar and the os magnum, the former maintaining its normal relation to the radius, and a second class in which the semilunar was dislocated anteriorly in relation to both the os magnum and the radius. He considered the second class as the true enucleation. He believed the type of luxation to be determined by the shape of the semilunar bone which had a variety of forms, and also by the strength of the ligaments as well as by the direction and force of the trauma. The author advised closed reduction in early cases in which the rotation of the bone was not complete. He warned of the possibility of injury to the median nerve in the manipulations.

AMPUTATIONS

Formation of the Gritti-Stokes Stump.—In thirty Gritti-Stokes amputations, Oehlecker⁸⁵ stated that he had fixed the patella to the femur by wedging it into an especially prepared mortise. He removed the cartilage from the under surface of the patella and shaped it into a square plug by means of a jig-saw. He then fitted this plug into a similarly shaped depression in the end of the femur. This method yielded a firm, painless end weight-bearing stump.

RESEARCH

Investigation of Adolescent Kyphosis.—Having been interested for several years in the subject of adolescent kyphosis and having published previous articles on the subject, Mau⁸⁶ undertook to reproduce the condition experimentally and reported the results. He sewed the end of the shortened tail of young rats beneath the skin, making a marked curve. The animals were killed and examined after different intervals. He found that definite changes developed in the epiphyseal cartilages; on the concave side, there was irregular proliferation and limitation of growth of the endochondral bone. The bony framework of the body underwent change and showed new formation of bony trabeculae, with

84. Ettorre, E.: *Chir. d. org. di movimento* 12:153 (March) 1928.

85. Oehlecker, F.: *Zentralbl. f. Chir.* 55:2250 (Sept. 8) 1928.

86. Mau, C.: *Ztschr. f. orthop. Chir.* 51:106, 1929.

the development of marginal proliferations such as are seen in arthritis; the body itself became wedge-shaped, with the apex toward the concave side. As a result of pressure atrophy, the margin of the epiphysis bordering on the concave side disappeared completely. Parts of the epiphyses showed necrotic changes. The author considered that the whole process was one of functional adaptation to a habitual curve and that the mechanism of these changes, which so closely resembled those seen in roentgenograms of patients with adolescent kyphosis, was one of circulatory interference.

Experimental Study of Muscle Atrophy.—Lippmann and Selig⁸⁷ produced muscle atrophy in rabbits by various means: immobilization of an extremity, section of a nerve, tenotomy and the production of an irritative arthritis. They found that atrophy due to immobilization alone was relatively small in degree and slow in onset as compared to that which followed arthritis, nerve section or tenotomy. They inferred that although arthrogenic atrophy had to be considered as an atrophy of disuse, it was not the result of immobilization but was caused by a reflex mechanism.

87. Lippmann, Robert; and Selig, Seth,: Surg. Gynec. Obst. **47**:512 (Oct.) 1928.

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OSTEITIS FIBROSA AND GIANT CELL TUMOR*

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WITH FOREWORD BY

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BALTIMORE

FOREWORD

First, I would like to acknowledge our indebtedness to Mrs. Carl Joerissen, of Washington and Paris, and to those former patients and friends who contributed to the fund that made this research possible.

These two research fellows, Dr. Charles F. Geschickter and Dr. Murray M. Copeland, in the Surgical Pathological Laboratory of the Johns Hopkins University, began an independent study of multiple myeloma during the early spring of 1927, their senior year in the medical school, and continued their research in the laboratory and in the library. These studies were published in the *ARCHIVES OF SURGERY* in the April, 1928, issue, page 807.

During this time, they reviewed the entire collection of bone material in the laboratory, and thus prepared themselves for the more intensive study of all lesions of bone and all benign and malignant connective tissue tumors, beginning in July, 1928. Two papers are ready for publication: this one on the nature of osteitis fibrosa and giant cell tumor, and a second one, on the round cell sarcoma of bone, often of alveolar character, which is now grouped under the name of Ewing's sarcoma. These two papers, therefore, contrast the benign type of bone lesions with the malignant tumors. A third paper on osteogenic sarcoma is in process of preparation, and in this third contribution, which is the result of six months' research by the authors, an attempt will be made to present the differential diagnosis of the different types of benign and malignant tumors of bone and soft parts clinically, roentgenographically and microscopically—a presentation that has never been thoroughly made before.

It is only just to record that these papers present the personal views of these two students, and anything original that is presented should be

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* Illustrations by Mr. Herman Schapiro.

credited to them. All that the laboratory did was to furnish them with the material for the study. It is my opinion that in these papers they have presented new, interesting and, I trust, correct pictures both of the nature of osteitis fibrosa and the giant cell tumor and of the nature of sarcoma, which not only will be valuable in the practical diagnosis and treatment of these lesions of bone in their earliest stage, but will form a basis for future progressive investigation.

I do not wish to anticipate in this introduction any of the statements made in the paper; I wish only to emphasize here and there some of the more important conclusions.

MALIGNANT GIANT CELL TUMOR

Although the authors are firmly convinced that osteitis fibrosa and the giant cell tumor are either identical or of natures closely allied, they have been unable, in the series of cases studied or in the literature, to find a proved case of malignancy arising in the benign bone lesion called osteitis fibrosa, which is situated in the shaft of bones of young persons. In spite of the fact that the age incidence of Ewing's sarcoma and of osteogenic sarcoma is the same as that of osteitis fibrosa, except that more cases of the malignant type are observed in persons more than 20 years of age, there is no evidence that these sarcomas develop in bone, the seat of osteitis fibrosa.

In the literature, there seem to be reported a few authentic and verified cases in which malignancy developed in a tumor involving the epiphysis of an adult which must be looked on as a benign giant cell tumor; that is, later in this benign giant cell tumor tissue, malignant sarcoma cells appeared, and gave rise to metastases in the lungs, in which also the giant cells were present. Together we studied all the cases in the literature and all the cases in our own series, and this research will be published later.

In the cases in which we have the material for study there occurred but one death from metastasis from a possible giant cell tumor of the epiphysis. In this case, the restudy of the sections of the original tumor classified it with the malignant variant of the giant cell tumor, of which we have had eight cases and only one of which metastasized. The other seven reacted as any giant cell tumor does. I think we can say here in anticipation of this publication that the danger of malignancy in a central tumor of the epiphysis which microscopically belongs to the giant cell group is so remote that one is justified in the conservative treatment by curetting or by x-ray radiation.

The histologic studies and illustrations presented in this paper by Geschickter and Copeland, I hope, will give surgical pathologists and pathologists a greater confidence in their ability to diagnose the giant cell tumor and to place it in the benign group. I have just visited a modern and thoroughly scientific surgical clinic in which the chief

surgeon is a well-trained surgical pathologist. Nevertheless, he presented to me a case in which, because of the microscopic sections, he feared malignancy in a giant cell tumor. The case offered a clearcut clinical and x-ray picture of a central tumor with an intact bone shell involving a condyle, or a little more, of the lower end of the femur. There had been an injury with a pathologic fracture, which had healed, and the curettement of the central tumor had followed some weeks after the healing of the fracture. The x-ray photograph therefore, showed a little formation of bone outside of the bone shell, and the microscopic section pictured in addition to the typical giant cell tumor, shown in the accompanying illustrations, young granulation tissue with cells of the morphologic type of the sarcoma cell, near islands of new bone formation, the result of the fracture. Unfortunately, the fear of malignancy in the giant cell tumor is still too prevalent, and only studies of this character will ultimately allay that fear. There should not be any difficulty in differentiating the variations in the typical giant cell tumor from the malignant variant (fig. A) and the fully developed sarcoma (fig. 21). It is important to emphasize here that the malignant tumors of the epiphysis are sarcoma developing in chondroma or myxoma. Ewing's tumor involves the epiphysis only secondarily from the shaft. The osteogenic sarcoma involving the epiphysis has an entirely different x-ray and microscopic picture. The metastatic tumor of the epiphysis is rare, but there should be no difficulty in differentiating giant cell tumor from metastatic carcinoma. The majority of bone aneurysms recorded in the literature were simply blood cysts with zones of giant cell tumor tissue in the epiphysis. In our series of cases there are but two bone aneurysms in which the tissue outside of the blood cavity, lining the bone shell, showed no evidence of the giant cell tumor. We have not observed a malignant aneurysm for more than twenty-five years,* and the tissue in the two cases is not sufficiently well preserved to allow an exact histologic diagnosis. Both these patients died of metastases. Their tumors may belong to the group we have designated as the malignant variant of the giant cell tumor, of which we have eight cases, in one of which death was due to metastasis.

This malignant variant of the giant cell tumor (fig. A), as stated before, can be easily recognized at the biopsy from the frozen section. I have no evidence that it should be treated any differently. The facts are these: One curetted in the upper end of the humerus eight years ago has not recurred; another has not recurred in three years; two have not

* Since this article was written, I have observed a third case of bone aneurysm in a child, aged 12. The roentgenograms showed a defect in the shaft similar to bone cyst, but the bone destruction suggested malignancy. At exploration there was a blood cyst surrounded by tumor tissue, microscopically osteogenic sarcoma. This roentgenogram of an osteogenic sarcoma resembles that of a bone cyst more than any other sarcoma that we have observed.

recurred on recent observations of one and two years since the curetting. In one case in which an amputation was done in 1905, the patient was living twenty-three years later. Two recurred. One was in the lower end of the fibula, which was resected in a few months, and the patient at the time of writing has been well for five years. The second was in the lower end of the femur; it recurred two years after curetting. The limb was amputated and the patient is living at the time of writing, six years afterward.

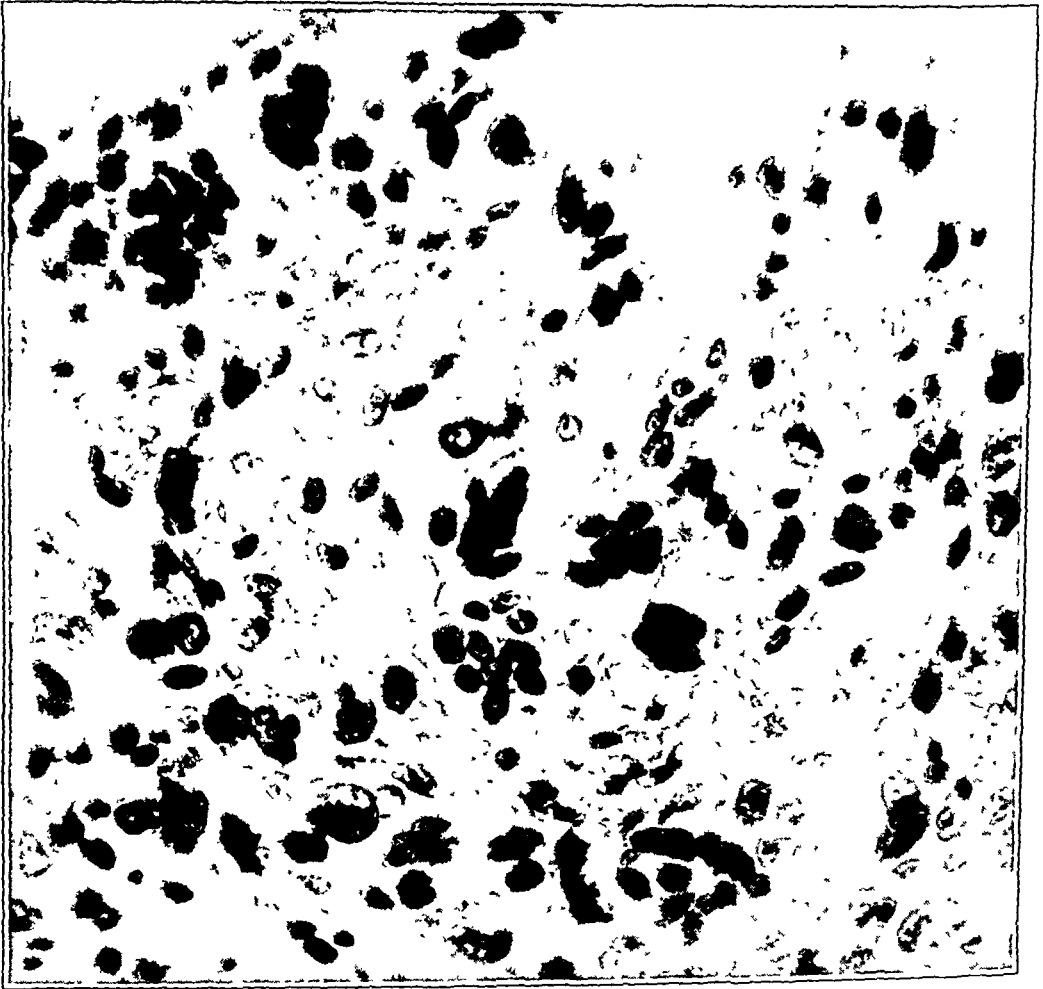


Fig. A.—The malignant variant of the giant cell tumor. Four large and several small giant cells are seen in the field. Among the small round cells of the stroma are larger cells with more cytoplasm and vesicular nuclei simulating sarcoma.

I am rather inclined to the view that if one finds a malignant variant of the giant cell tumor in the frozen section, it is wiser to resect and do a transplantation of bone, except in the lower end of the femur or the upper end of the tibia, where resection does not give as useful a limb as amputation and an artificial leg. Here one can try thorough curetting with chemical and thermal cauterization and irradiation to be followed by amputation if the tumor recurs.

To repeat, this small group of eight cases of the malignant variant of the giant cell tumor contains our only case of a supposed giant cell tumor which metastasized, and also shows a larger percentage of recurrences.

These eight cases of the malignant variant among 226 giant cell tumors were recognized by the authors when they first studied the microscopic sections without any knowledge of previous diagnosis or of clinical results.

RECURRENCE IN THE GIANT CELL TUMOR AFTER CURETTING

We have no record of a recurrence after resection. The only record of a recurrence in the stump after amputation was found in the literature, and in this instance the patient died of metastasis. The observation was made by Finch and Gleave of England and was reported in the *Journal of Pathology and Bacteriology* in the October, 1926, issue, page 329. We have thirty-two cases of recurrence after curetting. I presented the results of an investigation of the latter before the American Orthopedic Association in May, 1928, and the paper will be published in the *Journal of Bone and Joint Surgery*. From my studies, the chief factors in recurrence after curetting are: first, incomplete removal of the tumor, either because of hemorrhage or because of the inexperience of the operator; second, the failure to use chemical or thermal cauterization; third, attempting curettement when the bone shell is perforated or too much destroyed. There has been recurrence in the group with the latter condition in spite of thermal and chemical cauterization and in spite of preoperative and postoperative irradiation. I, personally, have had two cases which I have made the basis for my communication. The authors feel that in patients of more than 30 years of age, the danger of recurrence is greater than in younger persons, because the bone shell has lost its power to react and ossify.

RADIATION IN THE TREATMENT OF GIANT CELL TUMORS

Since my publication in the *Journal of Radiology* in March, 1920, I have repeated in every publication that it is wiser to put the doubtful bone lesions at rest and give x-ray treatment than to perform a biopsy, unless the operator or his pathologist has sufficient experience to make a differential diagnosis from the frozen section, and the patient is willing to have an amputation should the tumor prove malignant. Each year's experience confirms the truth of this. It is far safer to submit the x-ray photographs to others for help in diagnosis, employing radiation while waiting, than to perform a biopsy and send the section around for diagnosis.

In the past two years, the evidence has been increasing that persistent irradiation with x-rays or radium ultimately, in many instances, controls the giant cell growth. The tumor itself shrinks, and the x-ray

photograph shows increasing ossification. We are not yet prepared to make an exact comparison of the results after irradiation with those after curetting in properly selected cases. When we eliminate from our recurrent cases faulty curetting when the bone shell was intact and attempted curetting when the bone shell was destroyed, curetting has to its credit recoveries with perfect function in practically 100 per cent of the cases, and even if x-rays or radium could accomplish the same result in this group with intact bone shell, it would be more costly and take much more time. When the bone shell is destroyed, there is no question that irradiation should be tried first. Irradiation for recurrence after curetting is not so successful as irradiation without operation, nor has irradiation after recurrence following curetting prevented metastasis in the cases reported in the literature, notably the one reported by Ewing and Stone in the *ARCHIVES OF SURGERY* in 1923, page 289.

The question is, What is the danger of irradiation should the tumor be a chondrosarcoma or myxosarcoma? We have sufficient evidence to indicate that we may expect little or nothing of irradiation of the myxoma, or the chondroma, or the chondrosarcoma. The possibility of these tumors occurring in the epiphysis with x-ray pictures not unlike that of the giant cell tumor makes the problem difficult. In this malignant tumor of the epiphysis, the bone shell is usually partially destroyed. Therefore, from an x-ray standpoint, if the tumor is of the giant cell variety, the first treatment should be irradiation. I am not prepared to make any definite statement, but I am inclined to the view that, in doubtful cases, the nature of the lesion should be positively settled by a biopsy, provided the operator or his pathologist is competent to make a diagnosis. If not, irradiation should be the first method of treatment.

In conclusion, I want to call attention to the original view of the authors that osteitis fibrosa and the giant cell tumor are phases of bone repair; the first a healing reaction, the second an active vascularizing phase. In osteitis fibrosa, the tendency is to spontaneous reossification or healing. In the giant cell tumor this is not the case. Here the process leads to the formation of a mass of vascular tissue, in which giant cells predominate. The authors explain these different results with knowledge drawn from embryologic investigations of a new order.

Osteitis fibrosa and the giant cell tumor are specific lesions of bone and, in my opinion, are fundamental in all pathologic conditions of bone, just as chronic cystic mastitis is fundamental in all pathologic conditions of the breast, and, on the whole, is not unlike these benign lesions of bone in that it is a reaction of the parenchyma to some insult which, apparently, is not necessarily trauma, although trauma seems to be the starting point of osteitis fibrosa and the giant cell tumor. The authors also explain why osteitis fibrosa predominates in the shaft of bones in young persons and the giant cell tumor in the epiphysis of patients of a later decade.

CONTENTS

Introduction	176
Bone cysts	177
Clinical features	
X-ray features	
Gross appearance	
Microscopic analysis	
Nature of osteitis fibrosa	
Histologic Variants of the Bone Cyst.....	190
Giant cell variants of the bone cyst in the metaphyseal end of the long bones	
Polycystic osteitis fibrosa	
Giant Cell Tumor.....	197
Clinical features	
X-ray features	
Gross appearance	
Microscopic analysis	
Transitional Lesions Between the Giant Cell Tumor and the Bone Cyst.....	211
The spindle cell variant of the giant cell tumor	
Multiple giant cell tumor and multiple osteitis fibrosa	
Multiple giant cell tumor	
Multiple bone cysts	
The Nature of the Giant Cells.....	226
Varieties	
The relation of histogenesis of intracartilaginous ossification to giant cell tumors	
Giant Cell Tumors of the Skull.....	234
The chondrocranium in relation to giant cell tumors in the skull	
Giant cell tumors of the temporal fossa	
Giant cell tumors of the upper jaw	
Giant cell tumors of the lower jaw	
Epulis	242
Varieties	
Origin	
Xanthoma	249
Varieties	
Origin of xanthoma of the tendon sheaths	
The xanthoma variant of the giant cell tumor of the bone	
Giant cell tumors of the soft parts	
Subperiosteal Giant Cell Tumors.....	260
Etiology of Giant Cell Tumor.....	262
Relation of osteoclastasia to the interruption of the periosteal blood supply	
Embryonic histology in relation to pathologic changes.	
Summary	270

INTRODUCTION

Since the time of Galen¹ a form of lesion related to osteitis fibrosa and giant cell tumor has been known to medical writers under the term of epulis, a tumor of the alveolar border. But the increased discussion concerning etiology, beginning with Nélaton's² contribution to giant cell tumor in 1860, and Virchow's³ description of a solitary bone cyst in 1876, has failed to furnish a unified conception of the underlying pathologic processes of this group of lesions, despite the constant progress made.

In this paper an attempt is made to show that a single group of pathologic processes concerned in the repair of injured bone is responsible for this group of clinical entities. The classifications, therefore, of osteitis fibrosa, giant cell tumor, epulis of the alveolar border and giant cell tumor in the tendon sheaths of the xanthoma type have been regrouped on the basis of a fundamental relationship established by the observations reported in this article. The material on which this report is based was made available by Dr. Joseph Colt Bloodgood in the Surgical Pathological Laboratory of the Johns Hopkins Hospital, and this group of over 400 cases comprises an accumulation of gross specimens, microscopic sections, x-ray pictures, clinical histories and a system of case follow-ups for which his personal efforts during the past thirty-five years are largely responsible. In addition to the references noted elsewhere, we wish to make special mention of the recent and larger series of cases contributed by Stewart,⁴ Simon,⁵ Bloodgood,⁶ Ewing,⁷ Kolodny,⁸ Coley,⁹ Barrie,¹⁰ Lewis,¹¹ Codman,¹² Christensen,¹³ and

1 Galen, cited by Simon, W V. Die Knochensarkome, *Ergebn d Chir u Orthop.* **16**:364, 1923

2 Nélaton, E : *Tumeurs benignes des os*, Paris, 1860

3 Virchow, R. Ueber die Bildung von Knochencysten, *Monatsb d kgl preusz Akad d Wissenschaften zu Berlin*, 1876, p 369

4 Stewart, M J. The Histogenesis of Myeloid Sarcoma, *Lancet* **2**:1106, 1922

5 Simon, W V. Die Knochensarkome, *Ergebn d Chir u Orthop* **16**:364 1923

6 Bloodgood, J C. The Conservative Treatment of Giant Cell Sarcoma, *Ann Surg* **56**:210, 1912

7 Ewing, J. Neoplastic Diseases, ed 3, Philadelphia, W. B Saunders Company, 1928, p 314, fig 110

8 Kolodny, A. Bone Sarcoma, *Surg Gynec Obst* **44**:1 (pt 2) 1927

9 Coley, W B. Prognosis in Giant Cell Sarcoma of the Long Bones, *Ann Surg* **79**:321, 1924

10 Barrie, G. Haemorrhagic Osteomyelitis, *Am J Surg* **35**:253, 1921

11 Lewis, D D. Primary Giant Cell Tumors of the Vertebrae, *J. A. M. A.* **83**:1224 (Oct 18) 1924.

12 Codman, E A. The Nomenclature Used by the Registry of Bone Sarcoma, *Am J Roentgenol* **13**:105, 1925

13 Christensen, F C. Bone Tumors. *Ann Surg* **81**:1074, 1925

MacGuire and McWhorter¹⁴ on giant cell tumor and by Silver,¹⁵ Knaggs,¹⁶ Elmslie,¹⁷ Bloodgood,¹⁸ Morton¹⁹ and Konjetzny²⁰ on osteitis fibrosa from which valuable corroborative data were obtained.

BONE CYSTS

Clinical Features.—Although the limits of osteitis fibrosa have been widely extended since the time of von Recklinghausen²¹ to include a multiplicity of entities, the solitary bone cyst, which is a form of osteitis fibrosa found usually in the shaft of the long bones of young adults, presents certain uniform characteristics which allow this group of lesions to be discussed separately from a pathologic standpoint.

Von Mickulicz²² was among the first to observe that the age of a patient with a typical bone cyst is usually less than 21. Bloodgood,¹⁸ writing on this subject in 1910, called attention to the fact that the patient was generally less than 18, and Silver,¹⁵ in his review of ninety-seven cases in 1912, found only eighteen cases in which the patients were past the age of 20. In a review of bone cysts, Elmslie,¹⁷ in 1914, found a similar age incidence. In 175 cases of bone cysts in this series, the average age of the patients is between 10 and 15, although in about 20 per cent the patients are more than 21. This age distribution is one of the outstanding clinical features of the disease.

More noteworthy than the age incidence is the location of these tumors, for in the large majority of cases of solitary bone cyst the lesions are confined to three favorite sites, the upper shaft of the femur, the humerus or the tibia. In Silver's¹⁵ table of ninety-seven cases, the tumor was found in the femur in thirty-one cases, in the humerus in twenty-five and in the tibia in fifteen. Elmslie¹⁷ was

14. MacGuire, C. J., and McWhorter, J. E.: Sarcoma of Bone: An Analysis of Fifty Cases, *Arch. Surg.* 9:545, 1924.

15. Silver, D.: The So-Called Benign Cyst of the Bones, *Am. J. Orthop. Surg.* 9:563, 1912.

16. Knaggs, R. L.: The Inflammatory and Toxic Diseases of Bone. New York, William Wood & Company, 1926.

17. Elmslie, R. C.: Fibrocystic Diseases of the Bones, *Brit. J. Surg.* 2:17, 1914.

18. Bloodgood, J. C.: Benign Bone Cysts, Osteitis Fibrosa, *Ann. Surg.* 52: 145, 1910; *ibid.* 56:210, 1912; *ibid.* 69:345, 1919.

19. Morton, J. J.: The Generalized Type of Osteitis Fibrosa Cystica, *Arch. Surg.* 4:534 (May) 1922.

20. Konjetzny, G. E.: Die Sogenannte "Lokalisierte Osteitis fibrosa," *Arch. f. Klin. Chir.* 121:567, 1922.

21. Von Recklinghausen: Die Fibrose oder deformierende Osteitis die Osteomalacie und die osteoplastische Carcinose, *Festschr. zu Rudolf Virchow*, 1891.

22. Von Mickulicz: Discussion of case of Hans Haberer, *Centralbl. f. Chir.* 31:1323, 1904.

TABLE 1.—*Typical Bone Cysts*

Path. No.	Race, Sex, Age	Location*	Symptom†	X-Ray	Treatment	Microscope	Results
39030	W. F. 18	Humerus, shaft	Fracture	Cystic, expanded	Amputation advised
39258	W. M. 60	Tibia, upper	Fracture, 4 years	Expanded, perforated	Curetted	Typical osteitis fibrosa
39098	W. M. 10	Humerus, shaft	Tumor, 1 month	Cystic, expanded	Explored
38104	W. M. 8	Humerus, upper	Limp, 6 months	Cystic, deformity	Amputation	Osteitis fibrosa, bone formation
38074	W. M. 36	Femur, neck	Fracture, 1 year
37793	W. M. 2	Humerus, shaft
37624	W. F. 21	Femur, lower	Fracture, limp, 8 wks.	Cystic, encapsulated	Well 3 years
37618	W. F. 7	Tibia, upper	Tumor	Cystic, encapsulated	Curetted	Typical osteitis fibrosa	Healing 2½ years
37488	W. M. 16	Humerus, upper	Fracture, 2 weeks	Cystic, encapsulated
37146	W. F. 9	Radius, shaft	Fracture, pain, 3 mos.	Cystic, expanded
37114	W. M. 14	Femur, upper	Limp	Cystic, encapsulated
37062	W. F. 45	Radius, lower	Fracture, tumor, 2 yrs.	Ossifying cyst
36932	W. F. 22	Tibia, lower	Trauma	Ossifying cyst
36814	W. F. 21	Humerus, upper	Pain, 6 months	Cystic, encapsulated	Curetted
36850	W. M. 15	Humerus, lower	Fracture, 5 years	Large ossifying cyst	Osteotomy	Typical osteitis fibrosa	Well 6 months
36726	W. M. 4	Humerus, upper	Fracture, 6 weeks	Cystic, encapsulated	No tissue removed
36718	W. M. 17	Humerus, upper	Fracture, pain, 7 yrs.	Cystic, expanded
36692	W. M. 9	Femur, upper	Fracture, tumor, 6 mos.	Cystic, encapsulated	Inclined
36611	C. F. 4	Humerus, upper	Trauma, 1 week	Cystic, encapsulated	Curetted
36580	W. F. 15	Fibula, lower	Cystic, expanded	Operation advised
36518	W. F. 40	Femur, upper	Fracture	Cystic, expanded	Curetted	Typical osteitis fibrosa
26374	W. M. 10	Humerus, upper	Fracture	Cystic, expansion
36268	W. F. 36	Femur, lower	Tumor, 1 year	Cystic, expansion	Curetted	Recurred
36209	W. M. 7	Humerus, shaft	Trauma, 1 year	Expansion, fracture
36140	W. F. 12	Femur, upper	Trauma, 1 year	Cystic, encapsulated	Osteotomy, crushing	Typical osteitis fibrosa	Well 2 years
36000	W. F. 32	Femur, lower	Trauma	Cystic, expanded
35884	W. M. 5	Femur, upper	Tumor, 10 months	Cystic, expanded	Inclined
35814	W. M. 6	Tibia, upper	Trauma, 2 months	Cystic, expansion
35063	W. M.	Femur, upper	Trauma, 3 months	Cystic, expansion	Curetted
35006	W. F. 21	Femur, upper	Fracture, trauma, 5 months	Expanded cyst	Inclined
34482	W. F. 30	Tibia, lower	Pain, 18 months	Cystic	Inclined	Well 4 years
34374	W. F. 25	Femur, neck	Trauma, 3 years	Cystic, encapsulated	Curetted	Typical osteitis fibrosa	Well 1 year
33904	W. M. 9	Tibia, shaft	Tumor, 16 months	Cystic, encapsulated	Curetted
33236	C. M. 6	Humerus, upper	Trauma, 7 months	Cystic, expanded	Well 19 months
33006	W. M. 21	Femur, upper	Limp, 15 months	Cystic, expanded	Well 1 year

TABLE 1.—*Typical Bone Cysts—Continued*

Path. No.	Race, Sex, Age	Location	Symptoms	X-Ray	Treatment	Microscopic	Results
25542	W. F. 17	Tibia	Tumor, 12 years	Cystic, bending	Resection	Typical osteitis fibrosa	Well 3 years
25345	W. M. 17	Humerus, upper	Fracture	Encapsulated cyst
25109	W. F. 2	Tibia, lower third	Deformity, fracture	Fracture, rarefaction	Excision	Typical osteitis fibrosa	Well 9 years
24915	W. M. 4	Femur, upper	Fracture	Cyst with fracture	Well 3 years
24746	W. F. 15	Femur, lower	Trauma, 8 years	Cystic, expansion	Excision	Typical osteitis fibrosa	Well 3 years
24086	W. F. 24	Tibia, shaft	Tumor, 10 years	Expansion, encapsulation	Excision	Typical osteitis fibrosa	Well 3 years
24009	W. M. 5	Femur, upper	Trauma, 20 months	Cystic, expansion	Well 1 year
23617	W. M. 12	Femur, upper	Fracture	Cystic, expansion	Curetted	Typical osteitis fibrosa	Well 3 years
21911	W. M. 26	Radius, lower	Tumor, 10 years	Cystic, expansion	Curetted	Typical osteitis fibrosa	Well 10 years
20286	W. F. 26	Tibia, lower	Tumor, 5 years	Cystic, expansion	Excision	Typical osteitis fibrosa	Well 1 years
20209	W. F. 18	Femur, upper	Tumor	Inclined	Typical osteitis fibrosa	Well 5 years
20346	O. M. 35	Femur, shaft	Tumor, 5 years	Cystic, expansion	Amputated	Typical osteitis fibrosa	Well 7 years
16537	W. M. 8	Tibia, upper	Tumor	Cystic, expansion	Curetted	Typical osteitis fibrosa	Well 4 years
17433	W. F. 12	Radius, lower	Tumor	Cyst with fracture
16454	W. F. 5	Tibia, lower	Tumor, 2 years	Encapsulated cyst	Curetted	Typical osteitis fibrosa
16032	W. M. 20	Femur, lower	Fracture, 8 years	Encapsulated cyst	Well 3 years
16398	W. F. 3½	Tibia, lower	Tumor, 1 year	Healing cyst	Explored	Typical osteitis fibrosa	Well 9 years
14131	W. M. 16	Humerus, shaft	Pain, 1 month	Expansion, fracture	Curetted	Typical osteitis fibrosa	Well 7 years
13331	W. M. 16	Tibia, shaft	Trauma, 3 years	Expansion, encapsulated	Explored	Typical osteitis fibrosa
13829	W. F. 7	Femur, upper	Lump, 7 months	Encapsulated cyst	Excision	Typical osteitis fibrosa	Well 8 years
13593	W. F. 9	Humerus, shaft	Trauma, 8 days	Cystic, encapsulated	Curetted	Typical osteitis fibrosa	Well 10 years
13329	W. F. 8	Humerus, upper	Fracture, 10 days	Healing cyst	Excised	Typical osteitis fibrosa	Well 16 years
12231	W. M. 6	Humerus, upper	Fracture	Cystic, encapsulated	Curetted	Typical osteitis fibrosa	Well 9 years
16224	W. M. 5	Femur, upper	Tumor	Encapsulated cyst	Curetted	Typical osteitis fibrosa	Well 1 years
16474	O. M. 18	Humerus, upper	Pain, 3 weeks	Encapsulated cyst	Curetted	Typical osteitis fibrosa	Well 10 years
16275	W. F. 3½	Humerus, upper	Trauma, 2 years	Fracture through cyst	Curetted	Typical osteitis fibrosa	Well 12 years
9732	W. M. 18	Humerus	Fracture	Encapsulated cyst	Curetted	Typical osteitis fibrosa	Well 13 years
9568	W. F. 40	Fibula, lower	Tumor, 24 years	Encapsulated cyst	Curetted	Typical osteitis fibrosa	Well 2 years
9155	W. F. 21	Femur, lower	Trauma, 6 months	Encapsulated cyst	Amputated	Typical osteitis fibrosa	Well 10 years
9025	W. M. 13	Humerus	Tumor, 2 years	Encapsulated cyst	Curetted	Typical osteitis fibrosa	Well 10 years
8321	W. F. 21	Ulna	Tumor, 7 months	Encapsulated cyst	Well 2 years
8391	W. F. 11	Femur, lower	Tumor, 10 years	Cystic, expansion	Curetted	Typical osteitis fibrosa	Well 16 years
5533	O. F. 38	Femur, lower	Tumor, 1 year	Cystic, expansion	Amputated	Typical osteitis fibrosa	Well 20 years
5358	W. F. 7	Femur, upper	Trauma, 4 months	No note	Resected	Died of hemorrhage
4903½	W. M. 9	Humerus, upper	Fracture	Cystic, expansion	Curetted	Typical osteitis fibrosa	Well 50 years
3993	W. F. 7	Humerus, upper	Fracture, 1 year	Cystic, expansion	Inclined	Typical osteitis fibrosa	Well 17 years

impressed with the fact that the upper part of the femur and the upper part of the humerus were the prevalent locations for this type of lesion. The figures in our series are in accord with the observations of these authors. In 135 cases of solitary bone cysts, fifty-two were in the femur, forty-five in the humerus and thirty in the tibia. The fibula is next in frequency with eight lesions. In the cases in which the cyst was in the femur, thirty-two of fifty-two were present in the upper end, most of these being in the region of the greater trochanter. In the humerus, lesions in the upper end of the bone predominate, thirty-six of the forty-five cases in our series being in that locality, while in the tibia there is a similar predilection to involvement of the upper end. In all, about 75 per cent of these lesions showed a metaphyseal location in these three bones.

At the age and in the locality in which these tumors occur there is a relationship to an unossified epiphyseal line. The bone involved is therefore typically an area of new bone in a metaphyseal region. This fact would appear to relate the pathologic process involved to new bone formation, and in the microscopic study of these lesions, an attempt will be made to trace this relationship.

It is important to point out here that while the majority of bone cysts show this metaphyseal location, there is a fair percentage of them (16 per cent) which are found toward the region of the midshaft. This variation in site is explicable by the duration of the clinical symptoms. As will be seen from table 1, the average duration of symptoms is two and one-half years. In one fifth of the cases, the duration averaged ten years, and in several cases the patients had symptoms dating back from twenty to forty years. This long latent period preceding the diagnosis of the disease allows ample time for the affected area to progress gradually toward the region of the midshaft as the bone grows. In extreme cases in which from ten to forty years have elapsed, the reason for the occurrence of the bone cysts in patients more than 20 years of age is evident. Here the lesion takes the form of the so-called latent bone cyst discovered late in life as the consequence of some clinical incident leading to a roentgen examination, the previous presence of the tumor remaining unsuspected because of the absence of symptoms.

In accordance with this, a review of the histories shows that pain plays a mild rôle as a symptom of onset and that trauma with pathologic fracture or swelling is a more frequent cause in bringing the patient to the physician, pathologic fracture occurring in 45 per cent of the cases. In all cases we are impressed with the mildness of the clinical features, for only rarely is there extreme pain or marked bending deformity. The same facts are borne out by the clinical course which although protracted in many cases, is always benign, no patient ever dying from the direct cause of the disease.

X-Ray Features.—The typical x-ray picture of a bone cyst emphasizes many of the clinical features, the ununited epiphysis near the diseased area indicating the youthful age of the patient and the metaphyseal location of the lesions (fig. 1 *A*, *B* and *C*). A central area of bone destruction, which occurs most frequently in the upper part of the femur, humerus or tibia, casts little or no shadow in the roentgenogram and is crossed here and there by one or more trabeculations. About this area the cortex is thin and expanded to form a symmetrical and fusiform swelling. Often the bone is fractured at this site and along the margins of the fracture new bone formation casts a dense



Fig. 1 (nos. 35253, 34174 and 37796).—X-ray pictures of typical bone cysts in the localities most frequently affected: *A*, upper part of tibia; *B*, upper part of femur, and *C*, upper part of humerus. The lesions are near or at the metaphysis, and the ununited epiphysis in *A* and *C* indicate the youth of the patients. A pathologic fracture is shown in the upper part of the humerus.

shadow. These fractures tend to heal, and with healing the lesions frequently will ossify and disappear. When the diseased area persists for any length of time, however, the condition progresses toward the region of the midshaft.

The shell of bone about the affected portion is rarely perforated except by fracture. Often this portion of the bone is bowed or thickened. The new bone formation is then subperiosteal and cortical and produces no periosteal spicules, either parallel or radiating.

Gross Appearance.—The bone overlying the cyst varies in thickness according to the duration of the symptoms, the thicker shell encountered

in old cases indicating that a healing reaction is taking place (fig 2). A connective tissue lining is usually beneath the bone shell, and further toward the interior is the cavity which most frequently contains a serous fluid.

Bloodgood²⁸ has ably given a classification of the variations in the gross pathologic changes in these cavities or cysts. They may or may not have a connective tissue lining, and fluid or solid fibrous tissue may be found beneath. Calcium spicules like snow may be found on the inner side of the lining, or the remains of tissue resembling the grumous giant cell tumor may be disclosed.



Fig. 2 (no. 8324).—Gross specimen of a large bone cyst of ten and one-half years' duration in the lower end of the femur in a woman, aged 21. There is an unusually large amount of fibrous tissue and new bone formation in the cyst wall because of the age of the lesion.

In any event the contents of the cavity explored in the gross give little or no clue to an area of new cartilaginous bone such as the clinical features of age incidence and location would lead one to expect. In the shell of bone overlying the cavity, there is frequently a thickness and firmness extending into the fibrous lining which suggests the formation of new bone, but the location indicates that this is proceeding from the cortical region of the shaft rather than from a central metaphyseal location. Aside from this cortical reaction the gross specimens suggest a process of bone destruction rather than one of new bone formation.

Microscopic Analysis.—A microscopic analysis of the bone cyst, although adding much to our information concerning the pathologic

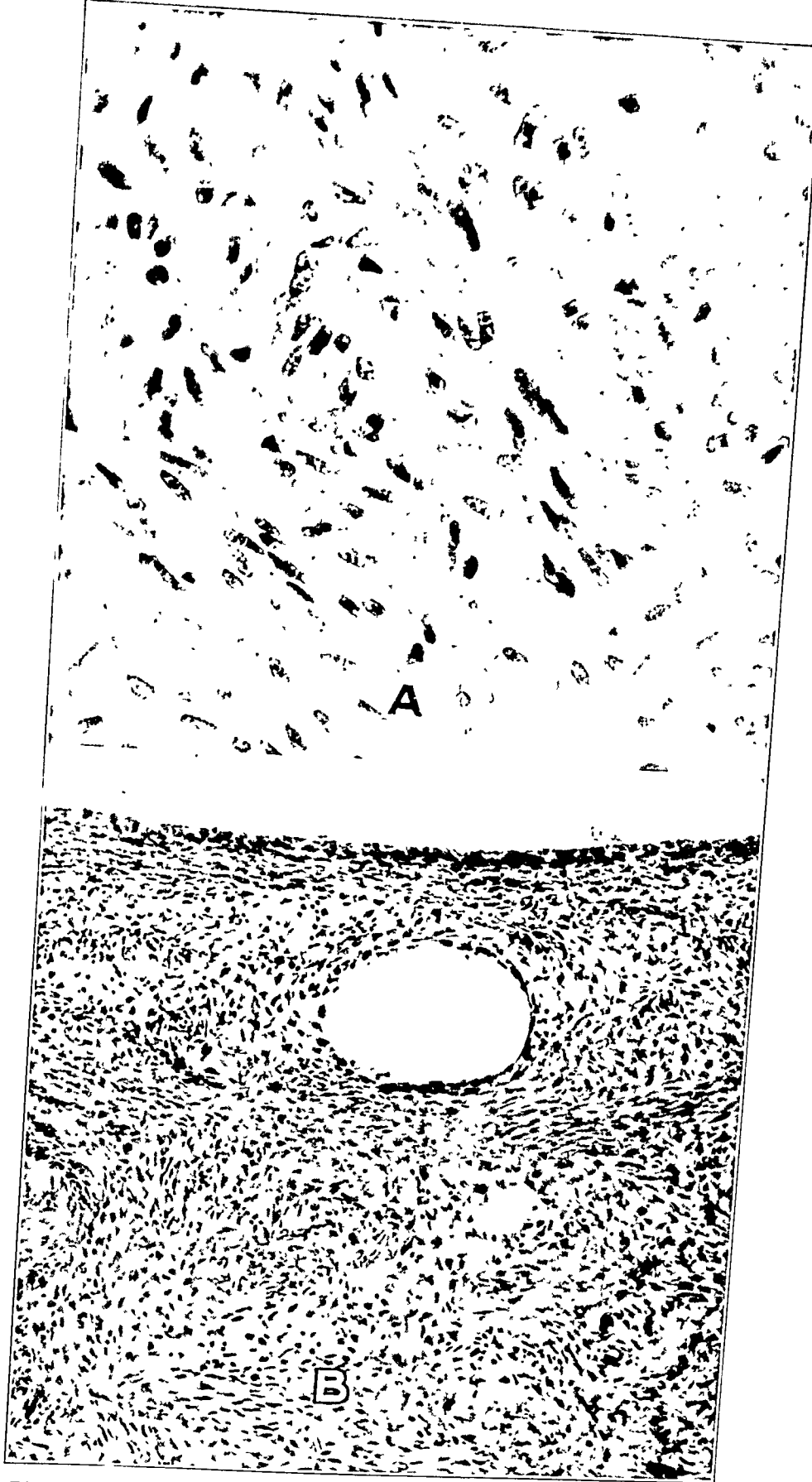


Fig. 3 (nos. 40124 and 24746).—Two typical areas of osteitis fibrosa. In figure *A* the intercellular substance is emphasized. In figure *B* there is condensation of fibrous tissue in the wall of the large cyst. A small cyst also is shown.

changes, fails to disclose in most instances a bone destructive process which would explain the cavity formation. Most of the tissue composing the cyst wall is fairly uniform and consists of spindle cells and fibroblasts among which there is much clear intercellular substance (fig. 3 *A*).

The tissue varies in relation to special areas. These special areas are of three main types: (1) cysts with or without old hemorrhage, (2) bone islands or bone trabeculae and (3) vessels in areas of fresh hemorrhage. Attention is first directed to the cyst wall. About the cyst wall there is a condensation of connective tissue to form a fibrous lining (fig. 3 *B*). Behind this lining layer embryonic fibroblasts are lay-



Fig. 4 (no. 19179).—*A* low and *B* high power of new bone formation in osteitis fibrosa. Osteoblasts derived from fibroblasts are laying down osteoid tissue. These spicules of new bone are characteristic of the process termed fibro-ostosis in this paper.

ing down intercellular substance, with the formation of osteoblasts and the direct proliferation of new bone. Occasionally, along the cyst wall or where two cysts walls meet with rupture in the wall, giant cell areas with round cells will be seen. Within the smaller cysts the remains of old hemorrhages are often found. In the larger cysts this is less likely to occur.

In regard to the substance around the bone spicules, the first or proximal row of cells is an actively proliferating layer of osteoblasts and numerous gradations between these cells and the fibroblasts (fig. 4 *A* and *B*). Beyond there is generally a loose fibrous tissue, almost myxomatous in appearance. Apparently, the process is from

spindle cell to fibroblast to osteoblast and then to bone formation, the bone at first being osteoid tissue previous to calcification.

Areas of fresh hemorrhage or new blood vessels present interesting features. Frequently an area with fresh blood will have a mixture of round and spindle cells in the neighborhood, or proximal to a new vessel will be seen a sprinkling of large giant cells of the epulis type (fig. 5). This relation of round cells and giant cells to spaces of red blood cells is most significant, and while some pathologists feel that giant cells are called on to absorb these hemorrhagic deposits (Konjetzny²⁰), it is important to emphasize that the giant cells are associated only with new vessels

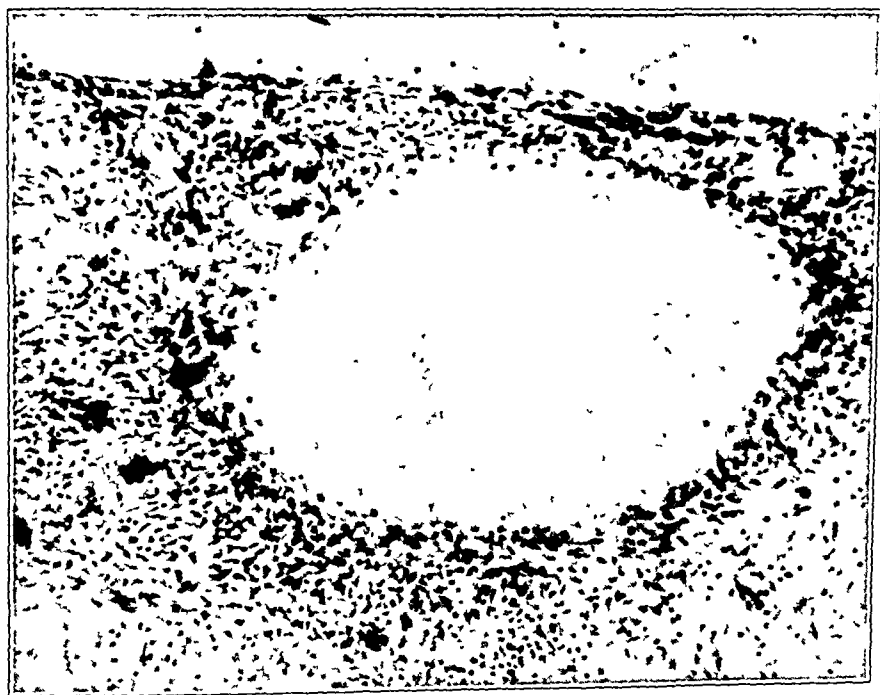


Fig 5 (no. 28609).—Photomicrograph from a bone cyst showing a newly formed cyst containing red blood cells and surrounded by a sprinkling of giant cells.

and fresh hemorrhages rather than with the old blood seen within the cysts. For this reason it is more probable that the order of pathologic events so far as microscopic analysis can disclose them is: (1) the formation of giant cell areas followed by new blood vessels and hemorrhage; (2) the absorption of hemorrhage with cyst formation, and (3) the lining of the cyst by fibrous tissue which is gradually transformed into bone. In any event the three processes of hemorrhage, cyst formation and new bone construction which represent the special areas in osteitis fibrosa seem to be related and to have a definite influence on the character of the adjacent stroma.

Minute areas of calcification are often seen in the new bone laid down in osteitis fibrosa. Bone via the cartilaginous route as seen in osteogenic sarcoma, however, has not been observed, neither has true myxomatous tissue. Although much has been spoken about myxomatous degeneration in osteitis fibrosa, the interpretation placed on such areas here is that they are loose embryonic connective tissue.^{22a}

Nature of Osteitis Fibrosa.—The foregoing analysis of the histology of the cyst wall in osteitis fibrosa leads to the conclusion that the process involved is essentially one of fibrous proliferation and new bone formation and therefore a repair or healing process. We do not see in this tissue evidence of an inflammatory reaction, although repair in bone following a medullary abscess may show the same healing phase typical of osteitis fibrosa.

In keeping with this view of the nature of osteitis fibrosa tissue, is the experimental work of Macewen²³ in his studies on the growth of bone. He found as we do in sections taken from numerous areas in the bone, that regeneration takes place independently of the periosteum. The patients suffering from the lesions considered here are in the younger period of life when (as Macewen has pointed out) the proliferating power of the bone cell is at its height. The bone involved by the disease reacts vigorously, and we find bone formation taking place through the activity of osteoblasts in a medium of fibrous tissue, without the transitory stage of cartilaginous calcification. The photomicrographs illustrated in this article, and indeed most illustrations of osteitis fibrosa, show an exact duplicate of the process depicted in Macewen's²³ book on new bone produced experimentally, growing inside of glass tubes.

The conclusion that areas of osteitis fibrosa represent a healing reaction in bone, attacks seriously the claim of osteitis fibrosa to consideration as a pathologic entity. In accordance with this view are the records of the grading files made during this study. Here diagnosis in the osteitis fibrosa group showed the largest percentage of error. Abscess walls, bits of capsule from central sarcoma of bone, or secondary metastatic tumor, and periosteum overlying ossifying hematoma or exostosis were all inadvertently placed among the sections classed as typical osteitis fibrosa. From a standpoint of microscopic diagnosis, it was a veritable dumping ground. The reasons for this are to be found in the non-specific nature of the tissue reaction, erroneously termed osteitis fibrosa. It is not an inflammation in fibrous tissue or in bone but a process of

22a. This loose embryonic connective tissue as pointed out by Leriche and Policard (Physiology of Bone, St. Louis, C. V. Mosby, 1928) is a pre-osseous edema pervading the connective tissue, and is always the first step in bone formation in this tissue.

23. Macewen, W.: The Growth of Bone, Glasgow, James Macelhose and Sons, 1912, figs. 27 and 28.

repair constituting a natural defensive reaction of cancellous bone, cortical bone and periosteum against pathologic invasion, whether the invading lesion is an abscess, a sarcoma or a giant cell tumor (figs. 6 *A* and *B* and 7).

In most cases of osteitis fibrosa this healing reaction is found around an evacuated area of bone destruction. The solitary bone cyst under

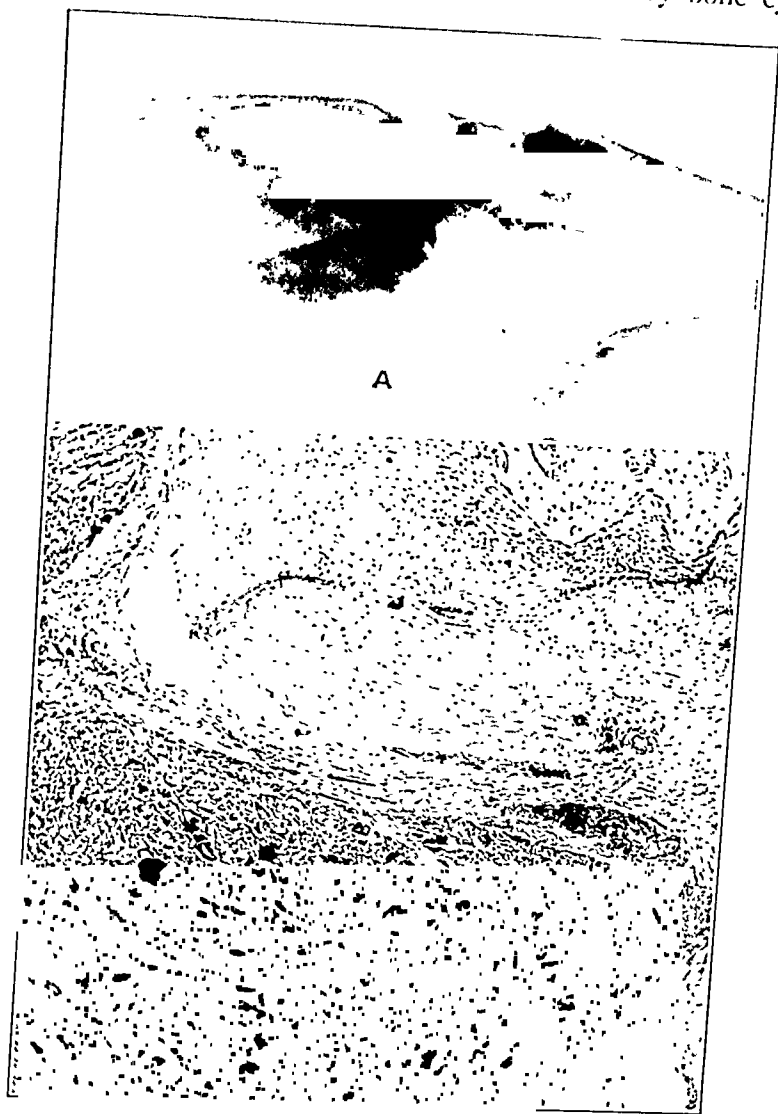


Fig. 6 (no. 36614).—Bone cyst formed about a foreign body. *A* is an x-ray picture and *B* is a photomicrograph from the same case. The patient was struck by a piece of flying steel eighteen months previously, the steel entering the hand. The superficial wound healed. Fourteen months later, swelling and pain occurred at the site of injury. The x-ray picture shows the cyst about the foreign body. The photomicrograph shows fibro-ostosis (new bone and fibrous tissue) surrounding an area of granulation tissue.

discussion shows such an area of bone destruction in the form of an enclosed cavity, and about it is the typical healing reaction which we believe is best termed fibro-ostosis (indicating new bone formed directly from fibroblasts). The reparative nature of this reaction of fibro-ostosis is evidenced clinically by the benign course of the disease and the tendency of the lesions to undergo spontaneous healing. Clinically and pathologically too, it would seem that the bone destructive process soon becomes arrested or often progresses without noteworthy symp-



Fig. 7 (no. 15745 [Bone Tumors: Group 9]).—Section taken from the margin of a Ewing's sarcoma of bone. The undestroyed bone is reacting to form a protective wall about the tumor, laying down new bone surrounded by osteoblasts. These new bone spicules with the surrounding fibrous tissue resemble osteitis fibrosa. A nest of round sarcoma cells is seen in the upper portion of the picture.

toms, for when we recognize the condition clinically and make the diagnosis or explore, the bone destructive phase is practically always complete and nothing is encountered but the healing phase. This fibroid process of repair sometimes extends over a period as long as forty-five years, and then a latent bone cyst is recognized. The persistence of the cyst beneath this healing reaction is due to nature's difficulty in collapsing

a cavity with rigid walls, and when fracture or a crushing procedure at operation aids in collapsing this cavity, the lesion heals.

HISTOLOGIC VARIANTS OF THE BONE CYST

The question arises as to what is the original bone destructive process in the bone cyst. In the average case the lesion is of two and one-half years' duration when first observed, and at the end of such a period the condition responsible for the area of bone destruction has disappeared. When bone cysts are grouped according to the duration of symptoms, however, and when the group in which the symptoms average six months are examined, we are able to discover by microscopic examination the nature of the process which forms this cavity in the bone. This group of early cases shows in the x-ray picture a metaphyseal location and a polycystic structure. Twenty-nine in the series of one hundred and seventy-five cases of bone cysts were in this group. Microscopically, they were all classed as giant cell variants of osteitis fibrosa. By this is meant that areas of large multinucleated giant cells embedded in a stroma of round cells, a tissue typical of a giant cell tumor, were always found in early cases of bone cysts examined pathologically. This confirms our microscopic analysis of the typical bone cyst, for as pointed out in the foregoing, there were histologic grounds for assuming that the giant cell areas preceded those of osteitis fibrosa.

In other words, we are inclined to the belief that the bone destructive phase of osteitis fibrosa is characterized by typical tissue of a giant cell tumor. More broadly stated, the average solitary bone cyst in the long bones is a healed or healing giant cell tumor. Not only do twenty-nine early cases of 175 cases of osteitis fibrosa show marked giant cell areas, but sixty cases of giant cell tumor of a series of 226 cases show a healing change toward osteitis fibrosa, most marked at the margins of the tumor but also infiltrating toward the center.

This does not mean that all bone cysts are healed giant cell tumors, nor is it true that giant cell tumors will all progress toward a healed state of osteitis fibrosa. In bone cysts 2 per cent of the cases can be shown to have a bone destructive phase due to a foreign body (fig. 6) or an abscess, and in about 20 per cent of the cases rather loosely classed as osteitis fibrosa some primary disease such as osteomalacia, Paget's osteitis deformans, fragilitas ossium, or osteo-arthritis is responsible for this cyst formation. The majority of solitary bone cysts (78 per cent), however, show their relationship to a preceding giant cell tumor phase (1) by the persistence of giant cell areas most frequent in the younger cysts with a shorter duration of symptoms, and (2) by the fact that these lesions are on the metaphyseal side of the epiphyseal line, bordering on the epiphysis in which giant cell tumors occur.

The polycystic group of osteitis fibrosa also emphasizes the relation of the bone cyst to giant cell tumor tissue, for in these lesions the small young cysts can be seen arising in giant cell areas and fusing together to form the larger cavities.

Detailed consideration of the lesions grouped under the variants of osteitis fibrosa in the metaphyseal ends of the long bones (table 2) and under the classification of polycystic osteitis fibrosa (table 3) brings out more forcibly the basis on which these conclusions rest.

Giant Cell Variants of the Bone Cyst in the Metaphyseal Ends of the Long Bones.—Clinically, these lesions are of shorter duration than

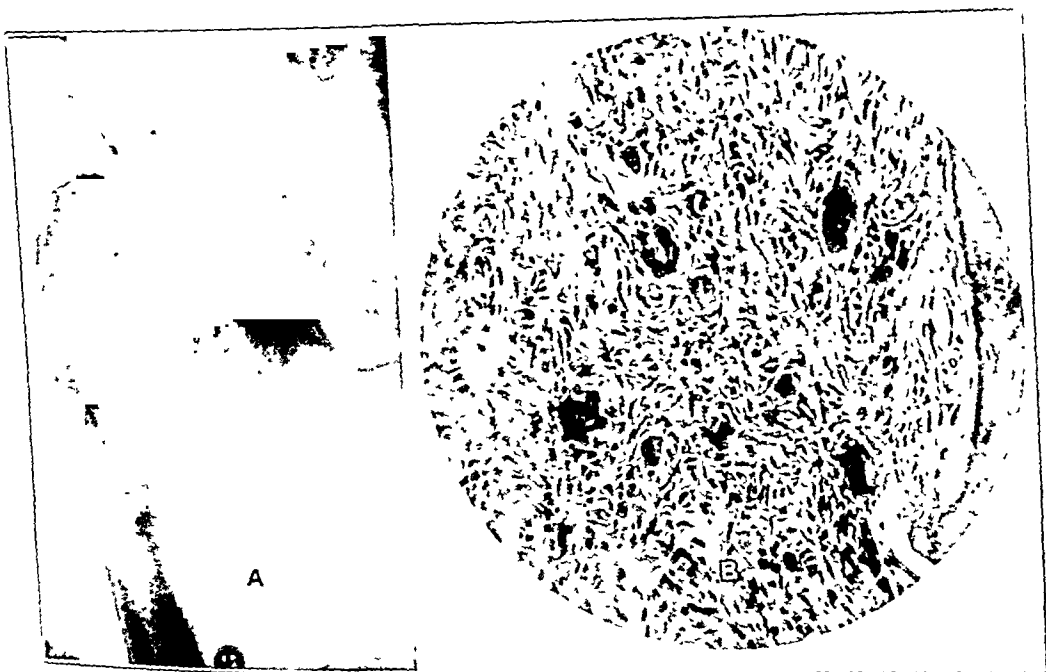


Fig. 8 (no. 17121).—Giant cell variant of osteitis fibrosa near an epiphysis. The x-ray picture, *A*, shows a lesion in the region of the greater trochanter which is inclined to be polycystic. There has been a pathologic fracture. The photomicrograph, *B*, from the same case shows numerous giant cells embedded in the stroma of osteitis fibrosa.

the typical bone cyst. The average duration in the group of cases tabulated in table 2 (with two exceptions) is six months. None of these lesions is found in the region of the midshaft, their location being invariably on the shaft side of the epiphyseal line, close to the area in which typical giant cell tumors occur. A favorite site for these hybrid bone cysts is the region of the greater trochanter in the femur, in which the condition occurred in six of the sixteen cases listed in the series (fig. 8, *A* and *B*). Here it will be recalled there is a separate epiphyseal line in youthful patients, which would seem to indicate that the trans-

TABLE 2.—*Variants of Osteitis Fibrosa in the Metaphysical Ends of Long Bones**

Path. No.	Race, Sex, Age	Location	Symptoms	X-Ray	Treatment	Microscopic	Results
40236	W. M. 10	Femur, lower	Trauma, 20 months	Shell perforated	Curetted	Giant cell areas in osteitis fibrosa	Discharged, well
35508	W. M. 15	Femur, condyles	Curetted	Giant cell areas in osteitis fibrosa	Discharged, well
35253	W. F. 5	Tibia, upper	Trauma, 10 weeks	Cystic, expansion	Curetted	Giant cell areas in osteitis fibrosa	Discharged, well
34490	W. F. 7	Tibia, upper	Trauma, 1 month	Cystic, expansion	Curetted	Giant cell areas in osteitis fibrosa	Well 1 year
34176	W. F. 14	Femur, trochanter	Pain, 1 year	Cystic, expansion	Curetted	Giant cell areas in osteitis fibrosa	Well 1 year
33882	W. M. 6	Femur, trochanter	Pain, 1 months	Cystic, expansion	Curetted	Giant cell areas in osteitis fibrosa	Well 4 years
32892	W. F. 27	Femur, trochanter	Trauma, 13 years	Polycystic, expansion	Curetted	Giant cell areas in osteitis fibrosa	Well 5 years
32013	W. M. 12	Femur, lower	Pain, 3 months	Cystic, expansion	Curetted	Giant cell areas in osteitis fibrosa	Well 3 years
19179	W. F. 31	Femur, lower	Trauma, 5 months	Cystic, fracture	Amputated	Giant cell areas in osteitis fibrosa	Well 5 years
18871	W. F. 23	Femur, trochanter	Pain, 6 years	Cystic, fracture	Curetted	Giant cell areas in osteitis fibrosa	Well 12 years
17121	W. M. 18	Femur, trochanter	Fracture	Polycystic, expansion	Curetted	Giant cell areas in osteitis fibrosa	Well 11 years
16297	W. F. 13	Tibia, upper	Trauma, 7 months	Cystic, expansion	Curetted	Giant cell areas in osteitis fibrosa	Well 9 years
15893	W. M. 5	Femur, upper	Trauma, 7 months	Cystic, fracture	Curetted	Giant cell areas in osteitis fibrosa	Well 11 years
10693	W. F. 19	Fibula, lower	Tumor, 11 months	Cystic, expansion	Resection	Giant cell areas in osteitis fibrosa	Well 5 years
10552	W. M. 12	Humerus, upper	Trauma, 2 years	Cystic, fracture	Curetted	Giant cell areas in osteitis fibrosa	Well 16 years
5614	W. M. 18	Humerus, lower	Pain, 2 months	Shell perforated	Excised	Giant cell areas in osteitis fibrosa	Well 5 years
						Giant cell areas in osteitis fibrosa	Well 21 years

* Lesions similar to those in this table but with marked polycystic structure are shown in table 3.

TABLE 3.—*Polycystic Lesions*

Path. No.	Race, Sex, Age	Location	Symptoms	Metaphysical Treatment	Location X-Ray	Microscopic	Results
37602	W. F. 19	Humerus, upper end	Trauma, 2½ months	Explored	Polycystic	Giant cell areas in osteitis fibrosa	Well 2 years
32581	W. F. 22	Tibia, malleolus	Trauma, 6 months	Curetted	Polycystic	Hemorrhagic cysts with giant cell areas	Well 3 months
29209	W. F. 12	Fibula, upper end	Trauma, 6 weeks	Resected	Polycystic	Small cysts surrounded by giant cell areas	Well 8 years
26053	W. F. 22	Finger, phalanx	Tumor, 6 months	Amputated	Polycystic	Hemorrhagic cysts surrounded by giant cell areas	Well more than 1 year
13211	W. M. 13	Femur, lower end	Tumor, 6 months	Resected	Polycystic	Multiple cysts with giant cells	Well 8 years
12207	W. F. 5	Tibia, upper end	Fracture, 16 months	Curetted	Polycystic	Small cysts surrounded by giant cell areas	Well 26 years
11166	W. M. 23	Tibia, malleolus	Tumor, 1 year	Curetted	Polycystic	Hemorrhagic cysts surrounded by giant cell areas, fibrous stroma	Discharged, well
5609	W. M. 21	Femur, trochanter	Fracture, 5 months	Curetted	Polycystic	Cysts surrounded by giant cell areas	Well 16 years
37250	W. F. 21	Humerus, Ulna, radius	Tumor, 3 years	Multiple Bone Involvement Explored	Polycystic	Small cysts surrounded by giant cell areas	Well 3 years
33358	W. F. 31	Humerus, Ulna	Trauma, 3 years	Curetted	Polycystic	Small cysts surrounded by giant cell and spindle cell areas	Unimproved
32732	W. F. 5	Tibia	Tumor, 3 years	Explored	Polycystic	Cysts surrounded by giant cell areas	Well 5 years
29831	C. M. 12	Tibia, fibula, foot	Trauma, 6 months	Curetted	Polycystic	Hemorrhagic cysts within giant cell areas	Discharged, well

formation of cartilage to bone taking place in this locality has some bearing on the pathologic process involved.

In the x-ray picture and in the gross this group of lesions is inclined to be more subcortical than central in location, and the structure is most frequently multilocular. When this polycystic character was particularly marked under the microscope, the lesions were grouped separately under the classification of polycystic osteitis fibrosa.

On microscopic examination the present group of cases of osteitis fibrosa contain giant cells which are smaller, have fewer nuclei and are more sparsely distributed than one would expect for a typical giant cell tumor located in an epiphysis. In the stroma, too, there are more fibro-

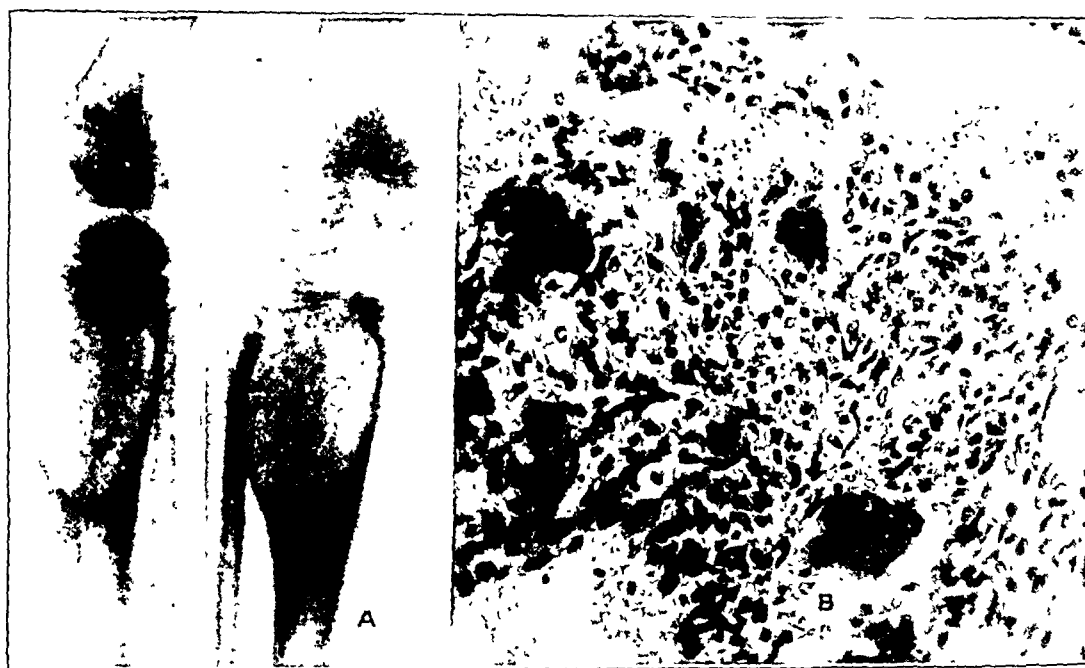


Fig. 9 (no. 34990).—A giant cell variant of osteitis fibrosa in the metaphysis (x-ray picture and section from the same case). *A*, the lateral and anterior x-ray views showing the typical fusiform lesion of the bone cyst extending to the epiphyseal line. The duration of symptoms was four months. *B* is a photomicrograph of one of the numerous giant cell areas found amid the osteitis fibrosa tissue in this lesion, demonstrating the tendency of the bone cyst to assume a giant cell structure when it borders on the epiphyseal line in an early stage of the disease.

blasts, more intercellular substance and more bone islands. However, small areas of larger giant cells surrounded by a narrow zone of round cells are met with here and there in the sections (fig. 9 *A* and *B*). Hemorrhages are a rather prominent feature of these lesions, and here the giant cells are apt to dispose themselves about the hemorrhage and about the cyst wall. The bone islands are the same as those found in osteitis fibrosa and are surrounded by osteoblasts.

The relation of this histologic picture to the relatively brief duration of the symptoms is again brought out by the recent cases referred to the surgical pathologic laboratory for diagnosis. Since patients have been consulting the physician more promptly during the last decade than ever before, sections from exploratory operations on bone cysts have shown, almost without exception, the inclusion of giant cell areas in the osteitis fibrosa tissue.

Polycystic Osteitis Fibrosa.—Two views may be taken concerning these lesions which are generally referred to by the name of polycystic osteitis fibrosa. One view is that they are an early stage of osteitis fibrosa, assuming a structure characterized by an aggregation of small cysts because a fusion of these small cavities at a later date represents the mode of origin of the large solitary cysts. The second view would be that such lesions are a more progressive form of bone cysts, and that their continued growth by the apparent budding of small cavities represents a transition between the solitary bone cyst (which is an arrested lesion) and the multiple form of osteitis fibrosa which is undoubtedly progressive. Some truth resides in both these views.

A survey of the cases in our series and those from the literature shows that in a large portion of cases the multiple bone cysts take on the structure of polycystic lesions. Hence, this peculiar multilocular structure is associated with the invasive nature of generalized osteitis fibrosa. On the other hand, when this polycystic structure is observed in a single bone (fig. 10 *A* and *B*), these lesions occur near the epiphyseal line in the metaphysis indicating an early stage in the transition from giant cell tumor to an arrested cyst. The most important feature, however, of this polycystic structure is that under the microscope these small cysts are surrounded by tissue rich in large multinucleated giant cells (fig. 31). This microscopic structure shows that elements of the bone destructive lesion of giant cell tumor persist and that the arrested stage characterized by fibro-ostosis and a scarcity of giant cells has not yet been reached. This lack of complete healing is explained on the one hand by the short duration of the symptoms and the proximity of the lesions to the epiphyseal line and on the other hand by the presence of multiple bone involvement indicating a generalized disease of the skeleton (table 3).

Knaggs,¹⁶ in his excellent review of osteitis fibrosa, stated that he was convinced that there is an earlier bone destroying stage in the pathologic process of bone cysts which is responsible for these lesions. He remarked, however, that he had never seen such an early stage nor a description of it in the literature. This early stage, we believe, is seen in all giant cell variants of osteitis fibrosa, and nowhere is it better exemplified than in this particular group of polycystic lesions known to



Fig. 10 (no. 28609) — *A*, polycystic osteitis fibrosa invading the epiphysis of the fibula; *B*, photomicrograph showing beginning of fusion in several small cavities. Note the association of red blood cells with the cysts.

the literature for over twenty-five years. The failure of the pathologic changes in this lesion to show its earliest stages has not been in the tumor but rather on the part of the pathologists in failing to recognize the significance of the histologic picture. This conclusion is justified by the appearance not only microscopically but also clinically. The duration of symptoms in this group of lesions when they occur singly near an epiphysis averages about five months compared to two and a half years for the typical bone cysts if one or two unusual cases are omitted. In the x-ray picture too, these lesions are found most often to be situated in a subcortical location rather than centrally, and this asymmetrical position is characteristic of both early giant cell tumors and early bone cysts as will be demonstrated later. From a histologic standpoint, the picture of multiple small cysts frequently filled by hemorrhage and sur-

TABLE 4.—Location of Typical Giant Cell Tumors

	Present Series*	Christensen's Series (Ann. Surg. 81: 1074, 1925)
1. Upper tibia.....	39	33
2. Lower femur.....	36	87
3. Lower radius.....	32	33
4. Lower ulna.....	9	13
5. Upper humerus.....	5	22
6. Lower tibia.....	5	9
7. Upper femur.....	5	11
8. Upper ulna.....	3	4
9. Upper fibula.....	3	12
10. Upper radius.....	2	1
11. Scapula.....	2	6
12. Rib.....	2	7
13. Lower fibula.....	1	3
Total.....	144	258

* All the lesions listed were in an epiphysis.

rounded by giant cells exhibited by this group of tumors has all the characteristics essential to the interpretation of it as a transitional form between the giant cell tumor and the bone cyst.

GIANT CELL TUMOR

Since an examination of the giant cell variant and polycystic forms of osteitis fibrosa leads to the conclusion that giant cell tumor tissue is the earliest phase in the pathologic process of bone cyst, an analysis of the typical giant cell tumor is in order. From its relationship to the bone cyst it is to be inferred that this typical giant cell tumor is an entity with a shorter duration of symptoms, with a tendency to involve bone newly formed from cartilage (in an epiphysis), and that it is primarily a bone destructive lesion with a slighter degree of healing reaction of the same "fibro-ostosis" character. Such inferences are confirmed by an analysis of more than 200 giant cell tumors reported in the following tables.

Clinical Features.—Clinically, the giant cell tumor is a progressive, bone destroying lesion occurring at any age in the epiphysis, where osteo-

TABLE 5.—Typical Giant Cell Tumor

Path. No.	Race, Sex, Age	Location *	Symptoms	Fracture	Treatment	X-Ray	Microscopic	Result
43765	C. F. 28	Femur, lower end	0	Curetting	Bone shell intact	Typical giant cell areas	Discharged well
42119	F. 14	Radius, shaft and upper end	0	Resection	Fibrous reaction at capsule	Discharged well
42429	W. F. 18	Tibia, right lower end	0	Curetting	Typical giant cell areas	Discharged well
40548	W. M. 23	Tibia, left upper end	Tumor 1½ years	0	Curetting	Bone shell intact	Typical giant cell areas	Discharged well
40163	M.	Radius, lower end	0	Curetting	Typical giant cell areas	Discharged well
40080	W. F. 18	Tibia, upper end	Tumor 2 months	0	Curetting	Bone shell intact	Typical giant cell areas	Discharged well
39052	W. M. 32	Tibia, upper end	Tumor 6 months	0	Curetting	Bone shell intact	Typical giant cell areas	Discharged well
39546	W. F. 25	Femur, right lower end	Pain 2 years	8 mos.	X-ray	Bone shell intact	Well less than 5 years
39454	W. F. 15	Scapula, left, neck	Pain	0	Curetting	Bone shell intact	Well less than 5 years
39242	W. M.	Ulna, right lower end	Trauma 3 months	0	Curetting	Fibrous reaction at capsule	Discharged well
39004	W. F.	Femur, lower end	Yes	Well less than 5 years
38570	W. F. 21	Radius, left lower end	Tumor 7 weeks	0	Curetting	Bone shell intact	Well less than 5 years
38976	W. F. 23	Femur, lower end, left	Trauma 8 months	0	Curetting	Bone shell intact	Well less than 5 years
38014	W. M. 32	Tibia, left upper end	Tumor	0	Curetting	Bone shell perforated	Typical giant cell areas	Discharged well
37953	W. M. 12	Femur, head	0	Exploration	Typical giant cell areas	Discharged well
37700	W. M. 21	Humerus, right upper end	0	Amputation	Bone shell intact	Typical giant cell areas	Discharged well
37360	W. F. 23	Femur, right lower end	Pain 8 months	6 wks.	Curetting	Bone shell perforated	Typical giant cell areas	Well less than 5 years
36440	W. F. 21	Tibia, left lower end	Pain 9 months	0	Refused	Bone shell intact	Discharged well
36410	W. F. 23	Femur, left lower end	0	Curetting	Bone shell perforated	Typical giant cell areas	Well less than 5 years
36353	W. F. 32	Tibia, right upper end	Trauma 22 months	Yes	Curetting	Bone shell perforated	Typical giant cell areas	Well less than 5 years
35902	W. F. 21	Radius, left lower end	Trauma 6 months	0	Exploration	Bone shell perforated	Discharged well
35892	W. M. 43	Tibia, left upper end	Trauma 18 months	0	X-ray	Bone shell perforated	Well less than 5 years
35704	W. F. 25	Fibula, left upper end	Tumor 13 months	0	Refused	Bone shell intact	Well less than 5 years
35362	W. M.	Tibia, left lower end	0	Amputation	Bone shell intact	Well less than 5 years
33464	W. F. 18	Femur, left upper end	0	Curetting	Bone shell intact	Discharged well
33114	W. F. 19	Femur, lower end	Pain 1 years	0	Exploration	Bone shell intact	Fibrous reaction at capsule	Well less than 5 years
33113	W. F. 40	Tibia, upper end	0	Curetting	Well more than 5 years
33102	W. F. 29	Tibia, lower end	Trauma 8 months	0	Amputation	Bone shell intact	Well 10 years
33100	W. F. 53	Femur, lower end	0	Curetting	Bone shell perforated	Well less than 5 years
33008	W. F. 29	Tibia, upper end	Tumor 3 months	0	Amputation	Bone shell perforated	Died of other cause
34090	W. F. 7	Tibia, left upper end	Trauma	0	X-ray	Bone shell perforated	Well less than 5 years
34574	W. F. 26	Ulna, lower end	Trauma 18 months	0	Curetting	Bone shell intact	Fibrous reaction at capsule	Well 5 years
34542	W. F. 57	Femur, upper end	Pain 5 months	Yes	Resection	Bone shell intact	Typical giant cell areas	Well less than 5 years
34248	W. F. 17	Tibia, right upper end	X-ray	Bone shell intact	Discharged well
34175	W. F. 14	Femur, upper end	Pain 1 year	0	Curetting	Bone shell perforated	Fibrous reaction at capsule	Well 5 years

31601	W. M. 36	Femur, right lower end	Pain 15 months	0	Curettung	Bone shell perforated	Typical giant cell areas	Well 5 years
31714	W. M. 26	Radius, lower end	Tumor 1 months	0	Curettung	Bone shell intact	Typical giant cell areas	Well more than 5 years
31760	W. M. 29	Tibia, left lower end	Pain 6 months	Yes	Amputation	Bone shell perforated	Typical giant cell areas	Well 5 years
31901	W. M. 27	Tibia, right upper end	Tumor 8 months	0	Curettung	Bone shell intact	Typical giant cell areas	Well more than 5 years
32001	W. M. 11	Tibia, left upper end	Pain 2 years	0	Amputation	Bone shell intact	Typical giant cell areas	Well more than 5 years
32277	W. M. 28	Tibia, left upper end	Pain 6 months	0	Curettung	Bone shell perforated	Typical giant cell areas	Well less than 5 years
32559	W. M. 25	Tibia, left lower end	Tumor 1 months	Yes	Curettung	Bone shell perforated	Typical giant cell areas	Well more than 5 years
33170	W. F. 62	Radius, right lower end	Tumor 2 years	0	Resection	Bone shell intact	Typical giant cell areas	Well 10 years
33921	W. F. 35	Scapula	Pain 18 months	0	Curettung	Bone shell intact	Typical giant cell areas	Well more than 5 years
33948	W. F. 27	Ulna, upper end	Tumor 6 weeks	0	Excision	Bone shell intact	Typical giant cell areas	Well more than 5 years
33315	W. F. 78	Radius, lower end	Tumor 6 years	Yes	Amputation	Bone shell perforated	Typical giant cell areas	Well 10 years
36256	Cl. M. 11	Femur, upper end	Tumor 10 months	0	Curettung	Bone shell intact	Typical giant cell areas	Well more than 5 years
36185	W. F. 23	Humerus, upper end	Pain 2 months	0	Amputation	Bone shell intact	Typical giant cell areas	Well more than 5 years
36187	W. F. 18	Tibia, right upper end	Tumor 2 years	Yes	Curettung	Bone shell perforated	Typical giant cell areas	Well 10 years
36172	W. F. 22	Tibia, left upper end	Tumor 8 months	0	Curettung	Bone shell intact	Typical giant cell areas	Well more than 5 years
36039	W. M. 28	Femur, lower end	Tumor 1 year	0	Resection	Bone shell perforated	Typical giant cell areas	Well more than 5 years
36718	W. M. 32	Radius, lower end	Pain 6 years	0	Curettung	Bone shell intact	Typical giant cell areas	Well more than 5 years
36715	W. F. 73	Tibia, upper end	Tumor 9 years	0	Curettung	Bone shell perforated	Typical giant cell areas	Well more than 5 years
36721	W. F. 38	Ribs, tenth posterior	Pain 1 year	0	Excision	Bone shell perforated	Typical giant cell areas	Well more than 5 years
36871	W. M. 29	Tibia, upper end	Tumor 6 months	Yes	Curettung	Bone shell intact	Typical giant cell areas	Well less than 5 years
36910	W. M. 31	Tibia, right upper end	Tumor 3 years	0	Curettung	Bone shell intact	Typical giant cell areas	No information
36909	W. M. 28	Tibia, left lower end	Tumor 1 year	0	Refused	Bone shell intact	Typical giant cell areas	Well more than 5 years
36934	W. F. 28	Radius, right upper end	Tumor 1 year	0	Curettung	Bone shell intact	Typical giant cell areas	Well more than 5 years
36931	W. F. 28	Radius, right upper end	Tumor 1 year	0	Curettung	Bone shell intact	Typical giant cell areas	Well more than 5 years
26384	M. 51	Femur, left lower end	Pain 9 months	0	Amputation	Bone shell perforated	Fibrous reaction at capsule	Discharged well
29129	W. F. 51	Tibia, right upper end	Pain 1 year	0	Curettung	Bone shell perforated	Fibrous reaction at capsule	Well 10 years
28872	W. M. 37	Ulna, right upper end	Pain 1 year	0	Curettung	Bone shell intact	Fibrous reaction at capsule	Well more than 5 years
28573	W. M. 12	Femur, left lower end	Pain 1 year	0	Curettung	Bone shell intact	Fibrous reaction at capsule	Well 10 years
28399	W. M. 35	Humerus, upper end	Pain 6 months	0	Amputation	Bone shell intact	Fibrous reaction at capsule	Well 10 years
28235	W. M. 35	Tibia, left upper end	Pain 1 year	0	Amputation	Bone shell intact	Fibrous reaction at capsule	Well more than 5 years
28107	W. F. 25	Tibia, upper end	Tumor 5 weeks	0	Amputation	Bone shell perforated	Fibrous reaction at capsule	Well 10 years
27807	W. F. 23	Femur, right lower end	Pain 1 year	0	Refused	Bone shell intact	Fibrous reaction at capsule	Well more than 5 years
27605	W. F. 20	Tibia, upper end	Pain 1 year	0	Resection	Bone shell intact	Fibrous reaction at capsule	Well more than 5 years
27601	W. F. 20	Tibia, upper end	Pain 1 year	0	Resection	Bone shell intact	Fibrous reaction at capsule	Well more than 5 years
27663	W. M. 45	Radius, left lower end	Tumor 19 months	0	Curettung	Bone shell perforated	Typical giant cell areas	Well more than 5 years
27318	W. M. 45	Tibia, upper end	Pain 6 months	0	Amputation	Bone shell perforated	Typical giant cell areas	Well more than 5 years
27116	W. F. 26	Femur, right lower end	Pain 6 months	0	Curettung	Bone shell perforated	Fibrous reaction at capsule	Well more than 5 years
27659	W. F. 26	Radius, upper end	Pain 6 months	0	Curettung	Bone shell perforated	Fibrous reaction at capsule	Well more than 5 years

* All the lesions listed were in an epiphysis.

TABLE 5.—Typical Giant Cell Tumor—Continued

Path. No.	Race, Sex, Age	Location*	Symptoms	Fracture	Treatment	X-Ray	Microscopic	Results
1	W. M. 30	Tibia, left upper end	Pain 16 months	0	Resection	Bone shell perforated	Typical giant cell areas	Well more than 5 years
2	W. M. 16	Humerus, left upper end	Tumor 16 months	0	Curetting	Bone shell intact	Typical giant cell areas	Well more than 5 years
8	W. M. 58	Ulna, right upper end	Tumor 1 year	0	Refused	Bone shell perforated	Well less than 5 years
9	W. M. 26	Tibia, upper end	Pain	0	Amputation	Bone shell intact	Well more than 5 years
9	W. F. 23	Tibia, upper end	Pain	0	Curetting	Bone shell intact	Typical giant cell areas	Well more than 5 years
7	W. F. 32	Femur, right lower end	Tumor 1½ years	Yes	Refused	Bone shell perforated	Well more than 5 years
1½	W. F. 32	Radius, left lower end	Tumor 1½ years	0	Resection	Bone shell intact	Well less than 5 years
7	C. F. 23	Ulna, lower end	0	Resection	Well more than 5 years
1	C. F. 33	Ulna, right lower end	Tumor 1 year	0	Resection	Bone shell perforated	Typical giant cell areas	Well less than 5 years
1	C. F. 41	Fibula, right lower end	Tumor 6 years	0	Curetting	Bone shell perforated	Well more than 5 years
½	W. F. 33	Femur, left lower end	0	Amputation	Well more than 5 years
1	W. M. 46	Femur, right lower end	Yes	Amputation	Bone shell perforated	Typical giant cell areas	Well 10 years
1	W. M. 11	Clavicle and first rib	Tumor 9 months	0	Resection	Well 10 years
1	C. F. 49	Radius, left lower end	Tumor 3 months	0	Resection	Bone shell intact	Fibrous reaction at capsule	Died of other causes
16720	W. F. 24	Radius, left lower end	Tumor 4 years	1 year	Resection	Bone shell intact	Typical giant cell areas	Well less than 5 years
16336	W. F. 24	Tibia, upper end	Tumor 18 months	0	Curetting	Typical giant cell areas	Well less than 5 years
16509½	W. M. 24	Radius, lower end	0	Curetting	Discharged well
14550	W. F. 24	Tibia, left upper end	Pain 6 months	0	Curetting	Bone shell intact	Well 10 years
14508	W. F. 19	Tibia, lower end	Tumor 2 years	0	Resection	Fibrous reaction at capsule	Well more than 5 years
14421½	W. M. 40	Femur, lower end	Tumor 5 years	0	Curetting	Bone shell intact	Well 10 years
13025	W. M. 34	Femur, right lower end	Pain 15 months	0	Curetting	Typical giant cell areas	Well 10 years
12927	W. M. 48	Radius, right lower end	0	Resection	Bone shell intact	Well 10 years
12474	W. M. 23	Ulna, right lower end	Tumor 8 months	0	Resection	Bone shell intact	Typical giant cell areas	Well more than 5 years
12776	W. M. 23	Tibia, left upper end	Pain 1 year	0	Resection	Bone shell perforated	Typical giant cell areas	Well more than 5 years
11855	W. F. 21	Fibula, right upper end	Tumor 7 months	0	Resection	Bone shell perforated	Typical giant cell areas	Well 10 years
11526	W. F. 21	Femur, lower end	Pain 2 years	0	Amputation	Bone shell intact	Typical giant cell areas	Well 10 years
10975	W. F. 26	Tibia, upper end	Pain 39 months	0	Resection	Bone shell intact	Typical giant cell areas	Well 10 years
9073	W. M. 24	Ulna	Tumor 20 months	0	Resection	Typical giant cell areas	Dead of other causes
8680	W. F. 72	Radius, right lower end	Tumor 8 years	0	Resection	Bone shell intact	Typical giant cell areas	Well 10 years
5666	W. F. 45	Femur, lower end	Pain 6 months	Yes	Amputation	Bone shell perforated	Typical giant cell areas	Dead of other causes
7831	W. F. 45	Femur, lower	Yes	Amputation	Bone shell perforated	Fibrous reaction at capsule	Well 10 years
6125	W. M. 22	Radius, lower end	Pain 20 months	0	Resection	Bone shell perforated	Typical giant cell areas	Well 20 years
6022	W. F. 52	Radius, lower end	Tumor 1 year	0	Refused	Bone shell perforated	Well 10 years
5601	W. F. 23	Femur, left lower end	9 yrs.	Amputation	Bone shell intact	Well 10 years
4394	W. F. 23	Femur, lower end	Tumor 3 years	Yes	Amputation	Bone shell intact	Typical giant cell areas	Well 10 years
5623	W. M. 23	Femur, left lower end	Tumor 6 months	Yes	Amputation	Bone shell perforated	Typical giant cell areas	Well 10 years
2458	W. M. 20	Femur, lower end	Tumor 1 year	0	Amputation	Typical giant cell areas	Discharged well
2420	W. M. 23	Radius, lower end	Tumor 7 months	0	Amputation	Bone shell perforated	Typical giant cell areas	Well 20 years
1915	W. M. 44	Radius, lower end	Pain 32 months	28 mos.	Amputation	Bone shell perforated	Typical giant cell areas	Well 20 years
738	W. M. 26	Radius, left lower end	Tumor 3 months	0	Amputation	Typical giant cell areas	Well 20 years
275	C. F. 45	Ulna, left lower end	Tumor 1 year	0	Resection	Typical giant cell areas	Well more than 10 years

* All the lesions listed were in an epiphysis.

genesis proceeds until late in life. The maximum number of cases (40 per cent) occur in the third decade between the ages of 21 and 31 years, or about a decade later than the average bone cyst. This is in keeping with the difference in locality of the areas affected. Whereas the bone cyst favors the metaphyseal ends of the upper part of the humerus, femur and tibia, the giant cell tumor selects most frequently the epiphysis of the lower part of the femur and radius and the upper part of the tibia (table 4). Ossification in the epiphysis persists later in life than in the metaphyseal regions and accounts for the age difference between these two tumors.

Although the giant cell tumor is typically benign, case follow-ups show thirty-two recurrences in a series of 226 cases indicating that the tumor is usually progressive and must be eradicated by proper treatment. Omitting five cases which gave the unusual history of a duration of from six to nine years, the average time when the patient first came under observation was fourteen months after the onset, as compared with the average for the typical bone cyst of thirty months. The usual sequence of symptoms was trauma, pain, tumor and fracture—trauma being present in 42 per cent of the cases and pathologic fracture in 14 per cent (table 5).

X-Ray Features.—The x-ray pictures of this tumor emphasize its bone destructive character. The lesion generally assumes an asymmetrical position in an epiphysis, a comparison of early and late lesions showing that the area of bone destruction begins in a subcortical location at one side of the epiphysis and works its way toward a more central location at the expense of cancellous bone (figs. 11, 12 and 13). The expanded bony shell of the tumor is extremely thin and, in slightly less than 100 cases examined roentgenologically in this series, was found perforated in 60 per cent of the lesions. Trabeculae traverse the diameters of the tumor when the shell of bone is intact, but as the tumor becomes larger, the trabeculae and then the bone shell disappear, the tumor extending into the soft parts. Such extension is aided by pathologic fracture when it occurs (fig. 14 *A* and *B*). In even relatively advanced lesions there is no periosteal reaction, and central areas of new bone formation are wanting.

Gross Appearance.—The gross appearance of the typical giant cell tumor shows the same bone destruction featured in the x-ray pictures, but demonstrates more clearly the limited but definite healing reaction about the margin of the tumor. The gross appearance of the tumor mass itself is usually hemorrhagic in nature. As Bloodgood stated, it is usually like an old bruise, every grade from red to black, although occasionally it is a uniform gray, putty color. At the operation, when touched, it bleeds, oozing like a sponge. When crushed, it is friable like

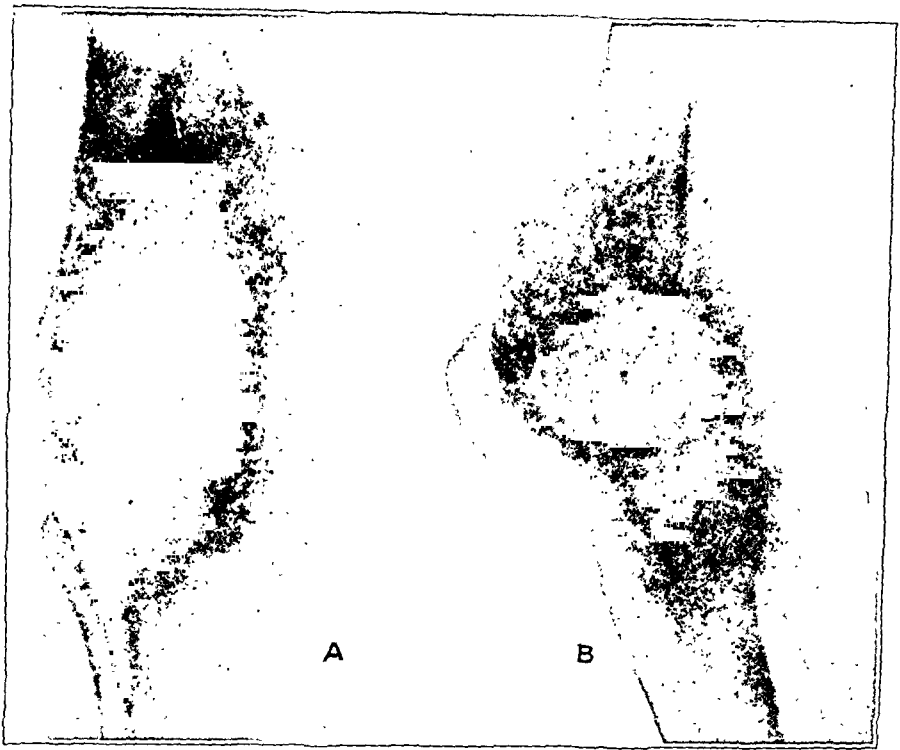


Fig. 11 (no. 25778).—*A*, anterior, and *B*, lateral x-ray views of a giant cell tumor in the lower end of the femur. Note the asymmetrical location of the lesion and the extreme thinness of the bone shell. The trabeculae have almost disappeared.

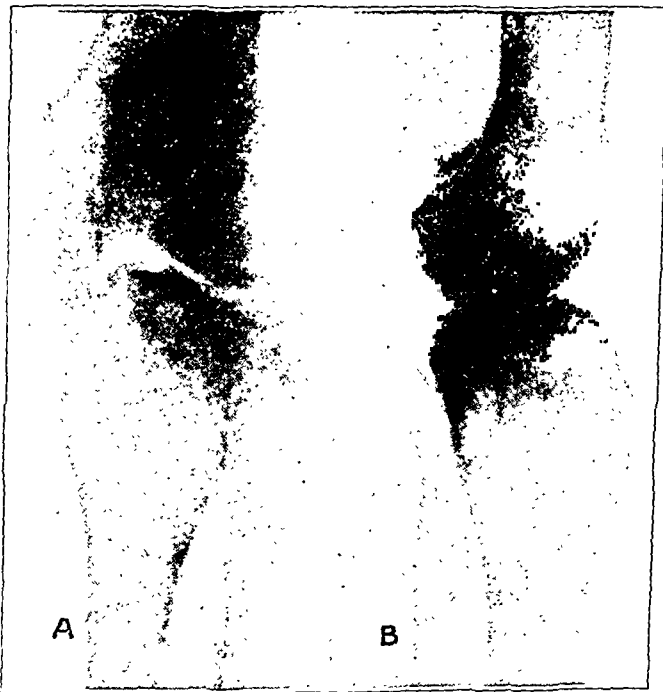


Fig. 12 (no. 32277).—*A*, anterior, and *B*, lateral x-ray view of a giant cell tumor in the upper end of the tibia. The bone shell is still intact; trabeculae are present.



Fig. 13 (no. 37708).—Giant cell tumor in the lower end of the right radius. The bone shell is perforated on the lateral side, and the trabeculae there are disappearing.



Fig. 14 (no. 37360).—*A*, x-ray picture, and *B*, gross specimen of a pathologic fracture through a giant cell tumor in the lower end of the femur. Fracture has aided the tumor in the invasion of the soft parts

cheese. Fibrous areas may be palpated in the gross, extending inwardly like partitions from the capsule. These are the trabeculae seen in the x-ray picture, and under the microscope they are fibrous septums resembling osteitis fibrosa.

The encapsulation of the tumor mass is sometimes effected by a connective tissue envelope, resembling in many respects the leathery fibrous capsule of the bone cyst. In the gross, the reaction of fibro-ostosis is most pronounced in the cortical bone on the shaft side of the epiphysis. Here the cortical bone thickens and extends downward from the shaft toward the epiphysis preceded by fibrous tissue. The cancellous bone extending across the medullary cavity on the shaft side also lays down a fibrous barrier to the tumor which may result in a capsule visible in the gross, but more often discernible only under the microscope when sections are made from this region.

In the epiphysis itself, in which the tumor is situated, the lateral margins present contrasting reactions. Because of its asymmetrical position the tumor borders on cortical bone on its outer side in early lesions, while inwardly, cancellous bone is infiltrated. The border of cortical bone resists longer and more effectively the advances of the tumor. Its reaction consists in the laying down of new bone and fibrous tissue (fig. 15 *A* and *B*). The natural structure of cortical bone, however, is extremely thin in this region of the epiphysis as will be seen from figure 16, and ultimate perforation through its wall is by no means rare. The superiority of its defense over cancellous bone is demonstrated, nevertheless, by the fact that the tumor expands centrally to the opposite side of the epiphysis in most instances before the cortical shell gives way. The joint cartilage, to which point the lesion generally extends because of its epiphyseal location, resists successfully the invasion of the joint cavity. Its defense is by means of calcification of its already compact substance, the calcified tissue being transformed into bone (figs. 17 and 18).

Thus it will be seen that everywhere about the tumor normal structures are endeavoring to stem the invasion. When this reactive tissue is examined microscopically, it shows a histologic structure typical of the fibro-ostosis seen in the wall of the bone cyst. Indeed the microscopic structure of the giant cell tumor differs from that of the bone cyst, not in kind but only in degree. Here there is more giant cell tumor tissue and less fibro-ostosis, while in the bone cyst there is a preponderant fibrous proliferation and new bone construction with little or no remnant of giant cell tumor tissue. Microscopically, these giant cell areas represent the fundamental pathologic change underlying these lesions, and a careful study of them discloses the nature of giant cell tumor.

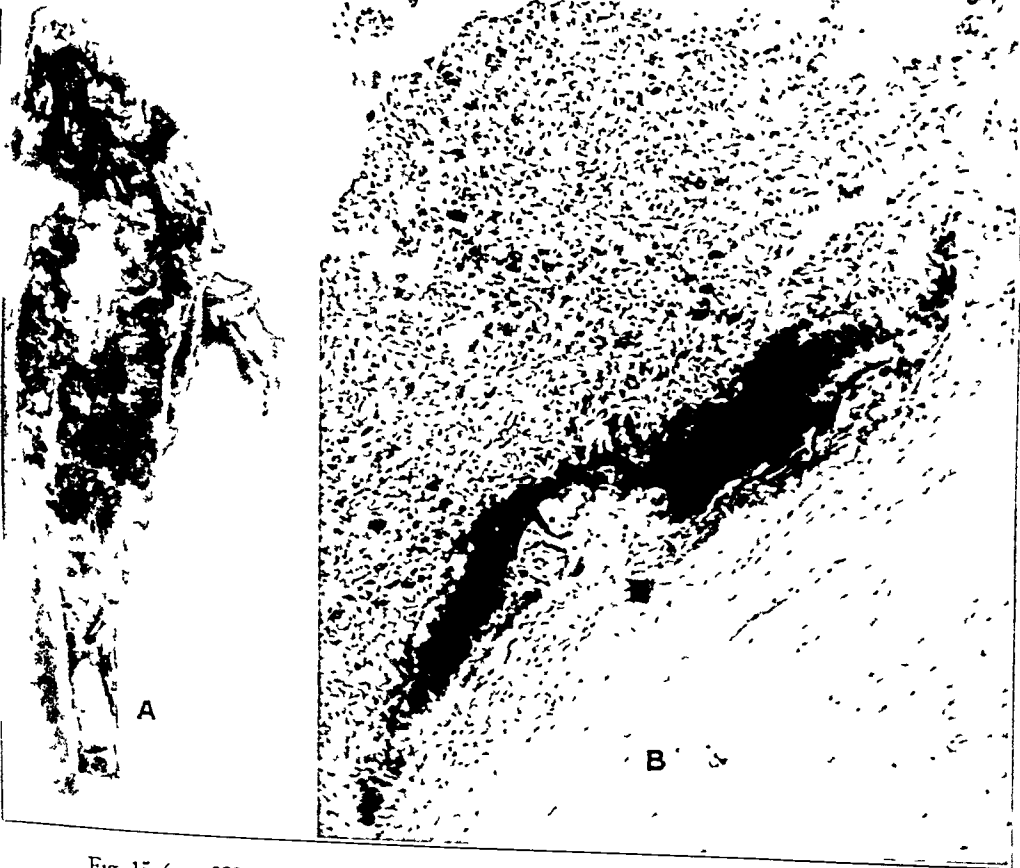


Fig 15 (no 32924) —*A*, gross specimen, and *B*, microscopic section of a giant cell tumor in the lower end of the fibula. The photomicrograph shows a reaction of new bone and fibrous tissue in the tumor capsule. The new bone has taken on a deep stain.

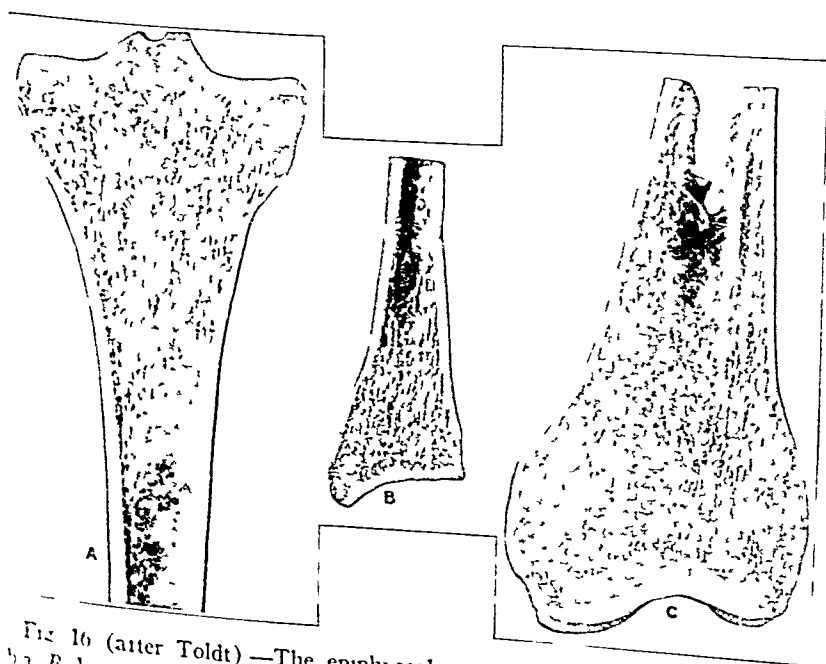


Fig 16 (after Toldt) —The epiphyseal regions of the *A*, upper part of the radius, *B*, lower part of radius and *C*, lower part of femur. Attention is directed to the normal cancellous structure of the epiphysis and the thinning of the cortex and compact bone and periosteum in these regions.



Fig. 17 (no. 27001).—Giant cell tumor in the upper end of the tibia. The tumor extends to the joint cartilage. No fibrous reaction is discernible here in the gross in the cut section. Fibrous tissue may be seen overlying the outer surface of the tumor on the uncut surface.

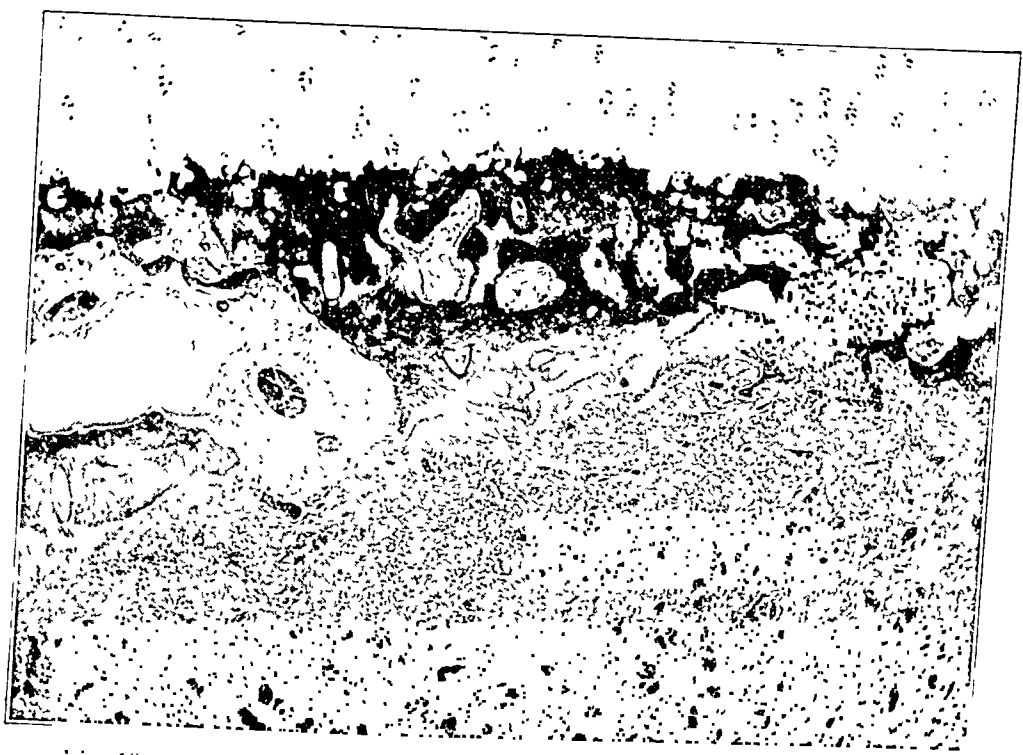


Fig. 18 (no. 10975).—Photomicrograph showing the reaction of joint cartilage. The cartilage has become calcified and is laying down compact bone to resist the invasion of the giant cell tumor.

Microscopic Analysis.—The tumor mass proper, of the typical giant cell tumor, which is responsible for the bone destruction observed in this lesion and also in the bone cyst, is composed essentially of large multi-nucleated giant cells embedded in a mass of smaller round cells (fig. 19 *A* and *B*). The giant cells average over 30 cells per field under the low power, with the number of nuclei in each cell varying from 15 to 200. The cells range in size from 10 to 100 microns and may or may not have distinct borders to the cytoplasm.

The number of giant cells present varies from field to field, being more numerous about areas of hemorrhage, about spicules of old bone or about the walls of minute cysts. The typical giant cell tumor, how-

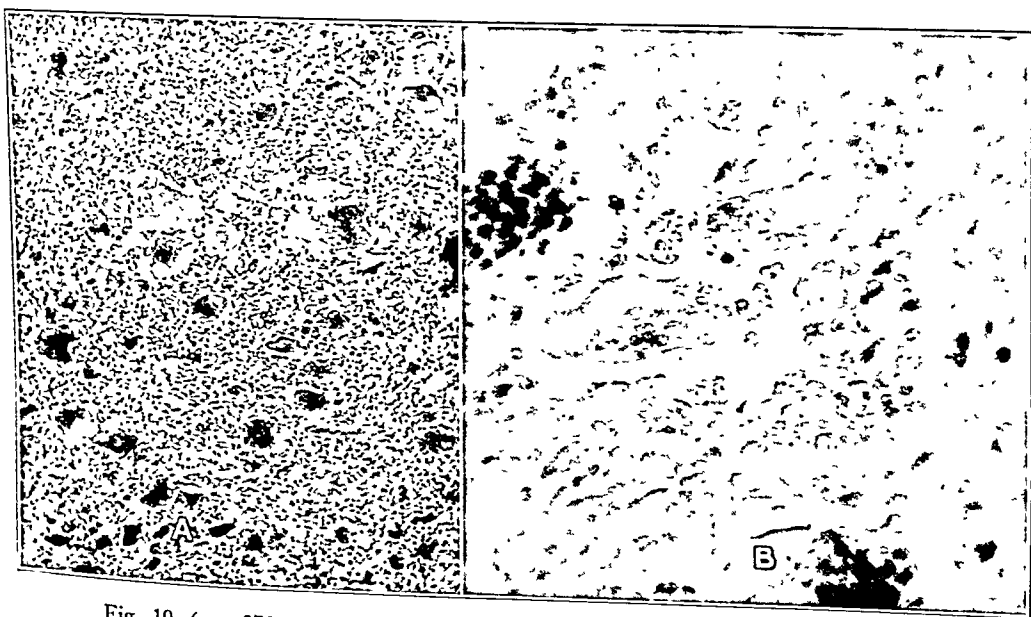


Fig. 19 (no. 37360).—*A*, low, and *B*, high power photomicrographs of the typical giant cell tumor. There are over thirty cells to the low power field and the usual number of nuclei is over fifteen per cell. In the high power it will be seen that round cells predominate the stroma.

ever, maintains with remarkable regularity, in most areas, a crowding of large multinucleated elements. Giant cells with few nuclei relatively small and sparsely distributed are not typical of the benign giant cell tumor and are more characteristic of the variants of osteitis fibrosa and osteogenic sarcoma (figs. 20 and 21).

An outstanding peculiarity of the typical giant cell tumor is the cellular stroma in which the giant cells are embedded. Two kinds of cells can always be found in this stroma, the round and spindle cell, but in the typical giant cell tumor group, the round cells outnumber the spindle cells in every instance. This small round cell has a relatively large nucleus and a small amount of cytoplasm. There is a definite

nuclear wall and a nucleolus. The nucleus is generally from 3 to 7 microns in size with a fairly large amount of chromatin evenly distributed, and the borders of the cytoplasm are usually indistinct.

There is, apparently, a definite relationship between the round cell of the stroma and the giant cell. In the first place, when the giant cell predominates the tumor by its numbers, the round cell prevails in the

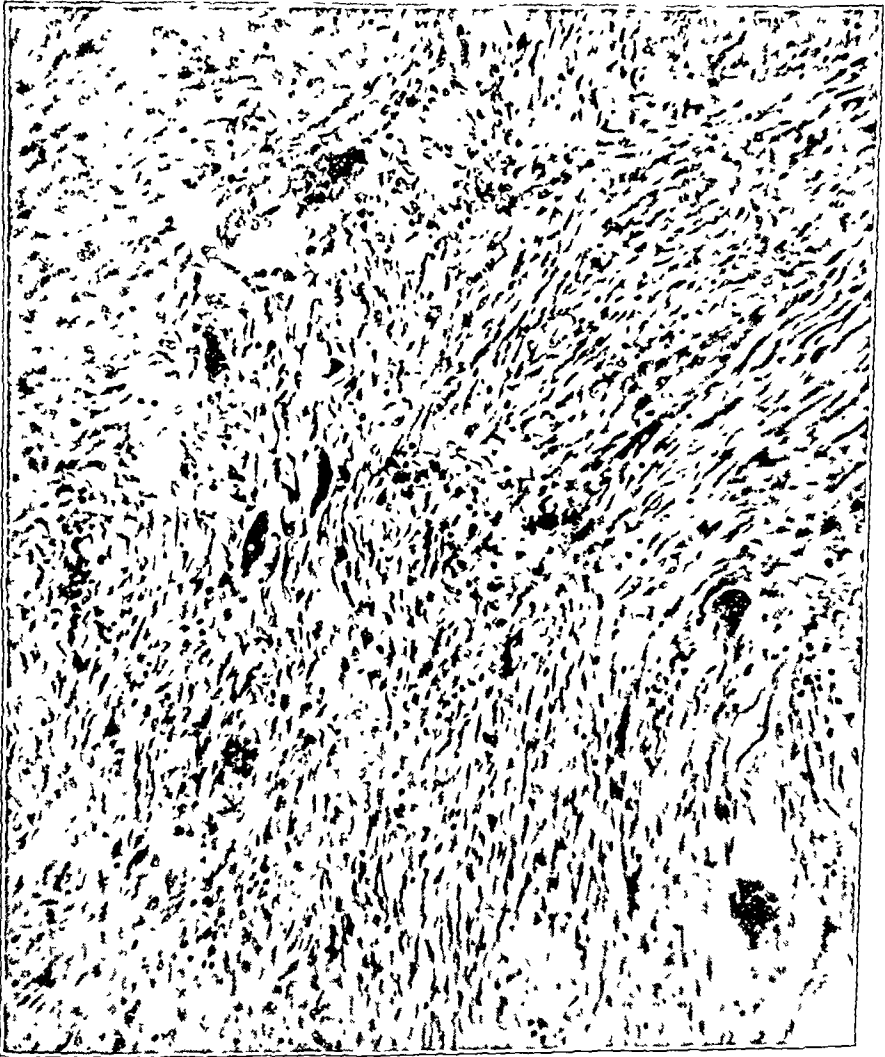


Fig. 20 (no. 32013).—The giant cell variant of osteitis fibrosa. Note the small size and scarcity of the giant cells and the large number of spindle cells and fibroblasts in the stroma. Microscopically, the tumor is benign.

stroma. Moreover, the nuclei of the giant cell always have the same general form and staining characteristics as the nuclei of the round cells. The only important variation is the tendency for the giant cells to have a more acidophilic cytoplasm with occasionally a greater concentration of chromatin in the nuclei and other signs of early degeneration. This

could be accounted for by a seniority in the age of the giant cell, the inference being that the giant cells are formed by agglutination of the round cells in the stroma.

Conspicuous in the histologic structure of giant cell tumor is hemorrhage. Red blood cells in a well preserved state infiltrate the tumor more often unenclosed by endothelial walls than otherwise. The typical

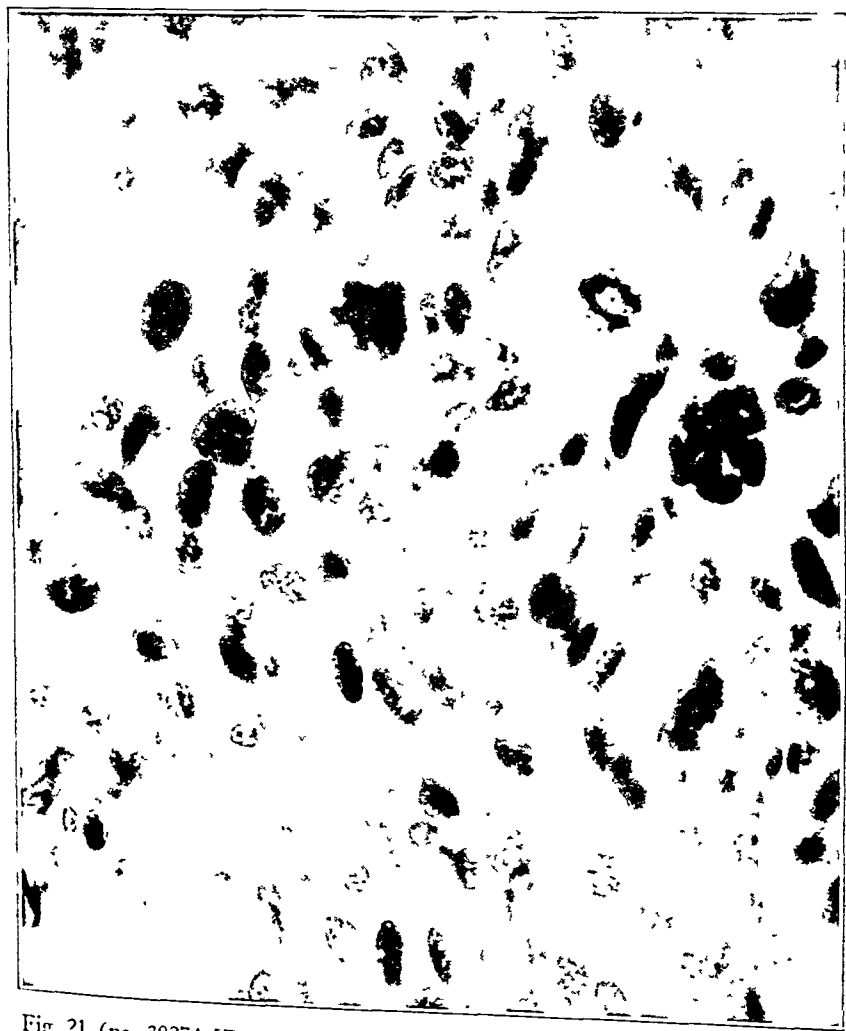


Fig. 21 (no. 39274 [B.T. 9]).—Osteogenic sarcoma with giant cells. Two giant cells are present in the field, each having less than fifteen nuclei. The most important diagnostic feature of the section is the presence of the large vesicular nuclei, some of which are undergoing mitotic division.

giant cell tumor is thus both hemorrhagic and vascular, newly formed vessels being by no means rare. Areas of organizing hemorrhage are frequent, and bordering on these is loose edematous tissue intermingled with areas of osteitis fibrosa.

Spicules of bone are frequently found near the margin of the tumor or at its capsule. Some of these spicules are undoubtedly surviving portions of old bone undergoing destruction (fig. 22), to be recognized by the giant cells applied to their surface, the condensation of calcium salts at the margins, the frayed and worn edges, and the small size of the bone cells included in the matrix of the spicules. Other spicules with osteoblasts applied to their surface are new bone resembling those fre-



Fig. 22 (no. 14229).—Spicules of old bone being attacked by giant cells. The margin of the spicules shows condensation of lime salts, worn and broken edges, and giant cell osteoclasts applied to the surface. The bone cells within the spicules are small, and fine linear markings are still present in the matrix.

quently seen in osteitis fibrosa, and represent a healing reaction rather than bone of tumor origin.

The spindle cells conspicuous about the new bone spicules are found elsewhere in the tumor among the round cells of the stroma. They are oval and slender in form with a nucleus rather well defined and a cytoplasm elongated but sparse, without definite outlines. Fine fibrils surrounding these spindle cells indicate their fibroblastic tendencies and

identify them with the same type of cells seen in osteitis fibrosa. When these spindle cells predominate the stroma in giant cell tumor, they indicate a healing process and mark the section as a variant (the spindle cell or osteitis fibrosa variant) of the giant cell tumor. This important group of hybrid tumors demonstrates a transitional phase between giant cell tumor and osteitis fibrosa.

TRANSITIONAL LESIONS BETWEEN THE GIANT CELL TUMOR AND THE BONE CYST

The so-called spindle cell variant of the giant cell tumor and the group of multiple giant cell tumors and multiple bone cysts demonstrate by their transitional structure the unity of the pathologic process underlying both the bone cysts and the giant cell tumor. These two transitional forms will be considered separately.

The Spindle Cell Variant of the Giant Cell Tumor.—It has been shown that the encapsulation of the giant cell tumor is accomplished by a healing reaction at its margin resembling in morphology, osteitis fibrosa. This healing reaction of fibro-ostosis predominates in sections taken from the margins of giant cell tumors, and for this reason twelve of the sixty cases graded as spindle cell variants of the giant cell tumor were found on further study to be taken from such areas in otherwise typical giant cell tumors. In this group of twelve cases a single section under the microscope would often show a giant cell area, a border of spindle cells, a further outlying zone of osteitis fibrosa and a final region of proliferating cortical bone, demonstrating clearly the nature of the healing reaction and the attempt by nature to lay down a defensive wall (fig. 23).

A special investigation was undertaken to verify this interpretation of the spindle cell tissue as a healing reaction. Blocks for sectioning were taken from various portions of the tumor margin in thirty gross specimens and examined. Sections taken from the region of cortical bone on the shaft side of the giant cell tumors always showed a marked protective reaction, histologically resembling in every respect fully developed osteitis fibrosa. The same was true of sections taken from a well formed connective tissue capsule, particularly where the periosteum joined in the formation of the capsule. When other sections were made from the region of cancellous bone either in the epiphysis or in the medullary cavity on the shaft side of the tumor, the defensive reaction was less pronounced but evident, and the infiltrating areas of giant cells in fibrous tissue gave the histologic picture typical of what has been called the spindle cell variant (fig. 24). Even when sections were taken at the point where tumor perforated and infiltrated into the soft parts, there was the same fibrous reaction, although under the microscope

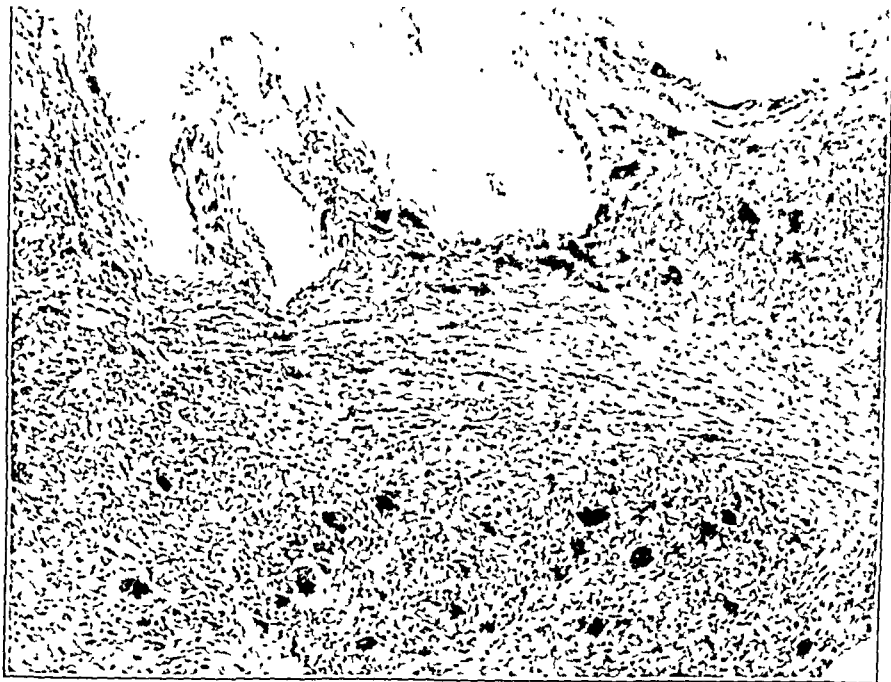


Fig. 23 (no. 17706).—Section taken from the periosteal margin of a giant cell tumor. New bone formation preceded by a layer of fibrous tissue is attempting to wall off the tumor.

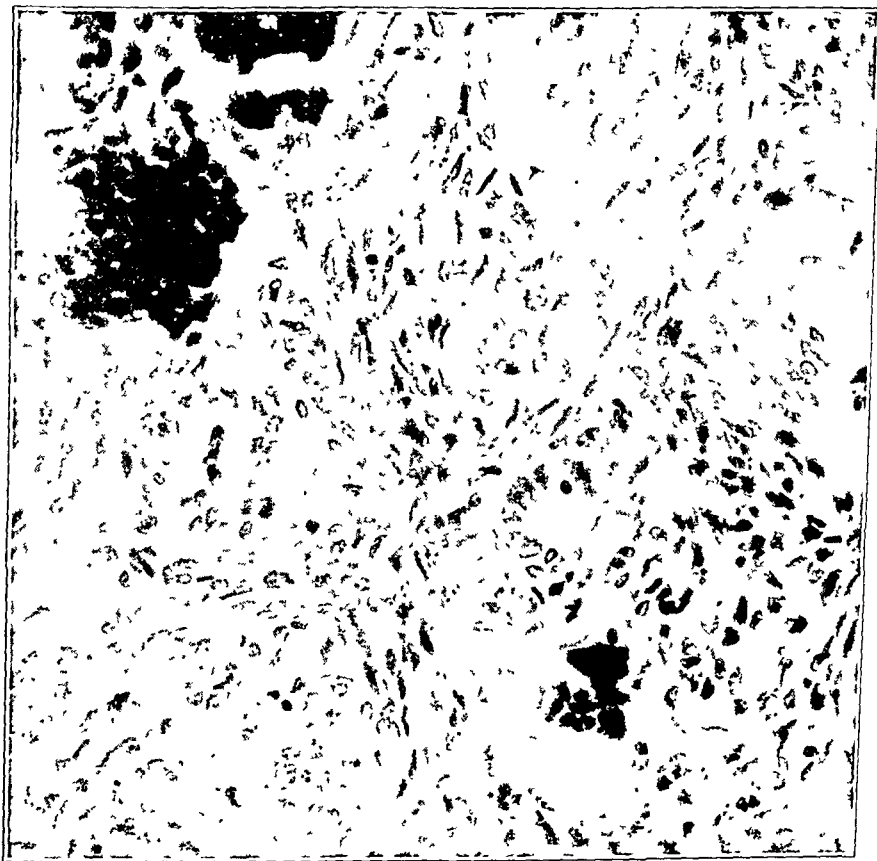


Fig. 24 (no. 11855).—A giant cell tumor showing spindle cell variation near the tumor margin. Spindle cells are infiltrating about the large giant cells.

avenues had been opened up in this tissue through which giant cells were streaming (fig. 25). Even on the cartilage side of the tumor margin toward the joint, the reaction was evident, calcified cartilage with transition to compact bone abutting on tumor area.

In thirty-seven cases showing this spindle cell variation under the microscope (tables 6 and 7), the fibroid change was fairly uniform throughout the tumor. This group of cases was of unusual interest because histologically it was practically impossible to make the distinction between giant cell tumor and bone cyst. Clinically, they were all

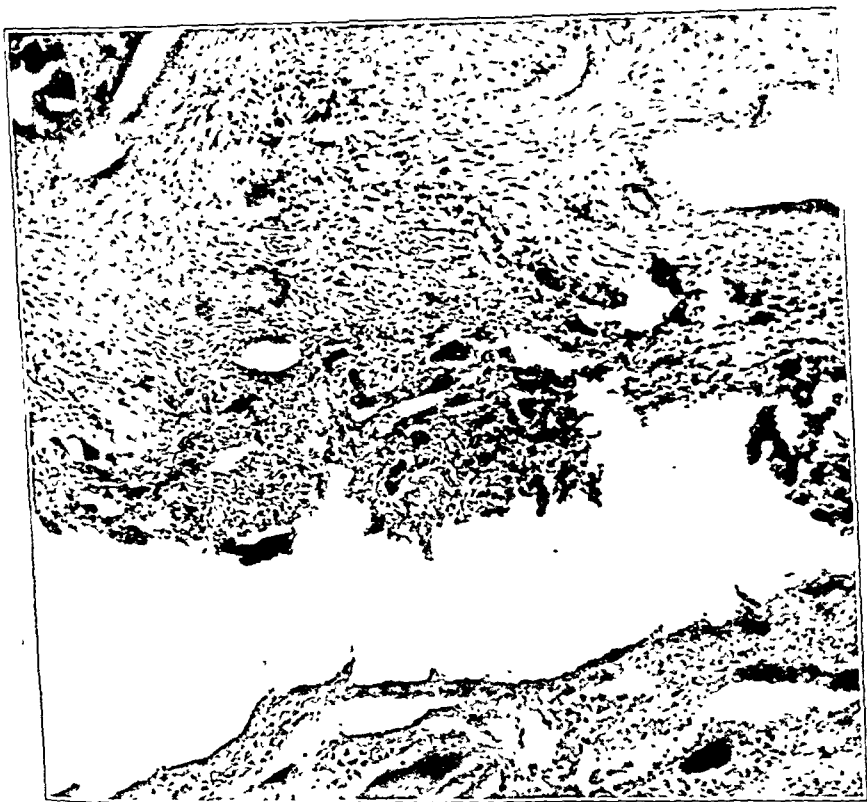


Fig. 25 (no. 26091).—Giant cells perforating the new bone of the tumor capsule. The channel in the lower portion of the picture is the line of perforation. The giant cells are deeply stained, and no definite structure is visible. The poor staining is due to the age of the specimen from which this particular area was selected for sectioning.

located in bones other than the long pipe bones, eight were in the vertebrae and twenty-nine were in the small bones of the hands and feet or in the flat bones. The interpretation placed on these lesions was that they represented giant cell tumors in which the healing reaction was unusually prominent. The clinical follow-up on this group of cases confirmed this. None of these patients died of tumor if we may except one which proved inoperable when a laminectomy was attempted on a

TABLE 6.—*Spindle Cell Variants of Giant Cell Tumors in the Small Bones*†

Path. No.	Race, Sex, Age	Location	Symptoms	X-Ray	Treatment	Microscopic	Results
23514	W. M. 60	Hand, phalanx	Pain 6 years	Bone shell intact	X-ray	Spindle cell stroma	Discharged well
35174	W. F. 30	Metatarsal, tarsal	Tumor 1 year	Bone shell intact	Curetted	Spindle cell stroma	Well less than 5 years
35110	W. F. 46	Hand, phalanx	Tumor 10 weeks	Bone shell perforated	Amputation	Spindle cell stroma	Well more than 5 years
32346	W. F. 10	Metacarpal, carpal	Tumor 6 months	Bone shell intact	Excised	Spindle cell stroma	Well less than 5 years
92909	W. F. 17	Metacarpal, carpal	Tumor 13 years	Multiple, encapsulated	Resected	Spindle cell stroma	Well more than 5 years
29103	W. F. 38	Metatarsal, tarsal	Tumor 10 months	Bone shell perforated	Amputation	Spindle cell stroma	Well less than 5 years
21052	W. M. 34	Metacarpal, carpal	No note	Multiple, encapsulated	Amputation	Spindle cell stroma	Discharged well
17536	W. F. 41	Foot, phalanx	Tumor 3 years	No note	Curetted	Spindle cell stroma	Well 10 years
17436	W. F. 26	Oscleis	Tumor	No note	Resected	No note	Well 5 years
17009	W. M. 30	Astragalus	Pain	Bone shell intact	Curetted	Spindle cell stroma	Well 10 years
16725	W. M. 33	Oscleis	Trauma 9 months	Bone shell perforated	Curetted	Spindle cell stroma	Well 10 years
21123½	W. F. 22	Vertebra, 5th lumbar	Trauma 8 months	Multiple, encapsulated	Curetted	Spindle cell stroma	Discharged well
33572	W. F. 22	Vertebra, 3d lumbar	Tumor	No note	Explored	Spindle cell stroma	Unimproved
33530	W. F. 16	Vertebra, 10th dorsal	Trauma 3 months	Bone shell intact	Resected	Spindle cell stroma	Well more than 5 years
30381*	W. M. 14	Vertebra, 4,5 lumbar	Trauma 7 weeks	No note	Curetted	No note	Well more than 5 years
29716*	W. F. 8	Vertebra, 2,3 dorsal	Paraplegia 1 month	Bone shell intact	Curetted	Spindle cell stroma	Well more than 5 years
20452	W. F. 11	Vertebra, 5th lumbar	Pain 5 months	No note	Curetted	Spindle cell stroma	Well less than 5 years
16307	Vertebra	Well when discharged
12838	W. M. 24	Sacrum, 5th lumbar	Paraplegia	No note	Explored	Spindle cell stroma	Dead of tumor
10634

† In table 7 are shown lesions of a similar nature, with a greater healing reaction.

TABLE 7.—*Giant Cell Variant of Osteitis Fibrosa in the Small and Flat Bones*

Path. No.	Race, Sex, Age	Location	Symptoms	Treatment	Microscopic	Results
36614	W. M. 28	Metacarpal	Tumor 4 months	Curetted	Osteitis fibrosa with giant cell areas	Discharged well
36152	W. M. 11	Metatarsal	Tumor 6 months	Resected	Spindle cell variant predominated by giant cells	Discharged well
35101*	W. M. 51	Vertebra, 4th dorsal	Paralysis	Laminectomy	Spindle cell variant predominated by giant cells	Well 1 year
31537	W. F. 31	Metacarpal	Trauma 16 months	Amputation	Spindle cell variant predominated by giant cells	Well 6 years
29690	W. F. 31	Patella	Trauma 13 months	Curetted	Spindle cell variant predominated by giant cells	Well 6 years
27628*	Metacarpal	Tumor	Excision	Cyst with giant cells	Well 7 years
27302	W. F. 4	Metacarpal	Tumor	Excision	Cyst with giant cells infected	Well 8 years
26953	W. F. 22	Hand, phalanx	Tumor 6 months	Amputation	Spindle cell variant with cysts and giant cells	Well 1 year
17049	W. M. 20	Astragalus	Trauma 1 year	Curetted	Cyst with giant cells	Well 6 years
15597*	W. M. 19	Hand, phalanx	Tumor	Amputation	Cyst with giant cells	Discharged well
10324	W. F. 19	Metatarsal	Trauma 3 years	Amputation	Spindle cell variant predominated by giant cells	Discharged well
28184*	W. F. 19	Pelvis	Trauma 5 years	Explored	Osteitis fibrosa with giant cells	Well 1 year
34166	W. M. 51	Rib, 10th	Trauma 15 months	Curetted	Giant cells against cartilage	Well 5 years
23674	W. F. 38	Pelvis	Pain 6 years	Resected	Spindle cell variant predominated by giant cells	Well 1 years
23911	W. M. 22	Pelvis	Trauma 2 years	Curetted	Osteitis fibrosa with giant cell areas	Well 6 years
21580	W. M. 72	Clavicle	Fracture 50 years	Excision	Osteitis fibrosa with giant cell areas	Well 9 years
12378	W. F. 72	Pelvis	Pain 1 month	Excision	Osteitis fibrosa with giant cell areas	Well 15 years

* Sections were not seen by the authors.

tumor near the sacral region. With this exception, the other patients are well without signs of recurrence whereas in the typical giant cell tumor, there is about 20 per cent of recurrence following similar treatment.

This group of lesions raises the question as to why the giant cell tumor of the epiphysis fails to heal and is a progressive lesion, while a similar tumor in the small or flat bones progresses partially toward healing and the bone cyst arising in the metaphysis of the long bones presents a predominately healing reaction. The explanation lies in the differences in the anatomic structure of the bones involved. The epiphysis is to be associated with the giant cell tumor, the metaphysis with the bone cyst and the small or flat bones with the spindle cell variant of giant cell tumor. The epiphysis in which the typical giant cell tumor occurs lacks the defensive mechanism represented by the thick cortex of the metaphysis and diaphysis of the long bones and the overlying periosteum which as Macewen²³ and Poland²⁴ have pointed out, is equipped in the shaft and the metaphysis with a rich and vascular osteogenic layer which is lacking in the epiphysis after the age of 3 years. Hence, the giant cell tumor progresses in the epiphysis, whereas the bone destructive lesion in the metaphysis is reacted to effectively by the cortical bone in that region, and as the bone grows, the cyst or tumor area in the metaphysis is pushed toward the region of the midshaft within the protective confines of the thick cortical bone as a walled-off cavity (fig 16). On the other hand, in the small bones, spacial limitations bring the developing tumor almost immediately into relation with cortical bone on all sides of the growth. An active defensive reaction against a giant cell tumor occurring in these bones is, therefore, set up early, and microscopically exhibits itself as a fibrous proliferation resulting in the so-called spindle cell variant. This early stimulation of compact bone on all sides of the lesion to produce fibro-ostosis makes it hard to find a region in a giant cell tumor of the small bones that is not invaded by young fibroblasts (figs. 26 *A* and *B* and 27 *A* and *B*). This tendency toward repair, however, although invoked early is not so marked as in the shaft of the long bones in which the cortex is thicker and more active.

The fact that lesions with characteristics of the giant cell tumor in small bones are often diagnosed as bone cysts demonstrates their healing tendencies. We feel, however, that the maintenance of two categories for diagnosis of these lesions in the small bones is unjustified. For years cases showing this type of tumor in the small bones have been shifted back and forth, classified first with bone cysts and then with giant cell tumor or vice versa, two independent classifications being maintained for a single pathologic entity. It is clear that these lesions are giant cell tumors, showing a fair degree of healing reaction when

24. Poland, J.: Traumatic Separation of the Epiphyses, London, 1898.

they have the appearance of a spindle cell variant and a further degree of healing reaction when they appear as osteitis fibrosa with giant cell areas. Certainly they are not the mythical entity of a cyst in the small bones secondarily invaded by giant cells.

Dean Lewis¹¹ in his paper on "Giant Cell Tumor of the Vertebrae" approaches this point of view. In this contribution Lewis reviews seven-



Fig 26 (no. 17436).—Giant cell tumor in the os calcis. The x-ray picture, *A*, shows mottling and bone destruction. The shell of bone is intact. The microscopic structure, *B*, shows a spindle cell variant of the giant cell tumor.

teen cases including one of his own, pointing out that recovery after partial removal or exploration only, has been noted in thirteen of the seventeen cases, ossification occurring relatively frequently. In his series, the condition in two cases was located in the transverse processes of the lumbar vertebrae, two in the lamina of dorsal vertebrae and the

majority of the remainder (as far as can be determined from the case reports) in the lateral portions of the vertebral body next the lamina. As will be seen from figure 28 the site of these vertebral tumors in the region of compact bone and the early defensive reaction of fibro-ostosis produced, accounts for the healing emphasized by Lewis. Fortunately, sections from one of Lewis' cases are in the laboratory, and like the six of our own (fig. 29) the sections show spindle cell variation. Perforation and extension into neighboring bones occur more frequently in giant cell tumors of the spindle cell group (twelve of seventeen in Lewis' series), but this is only because they so frequently occur in small or flat bones in which the cortex is always thin and other bones are in close

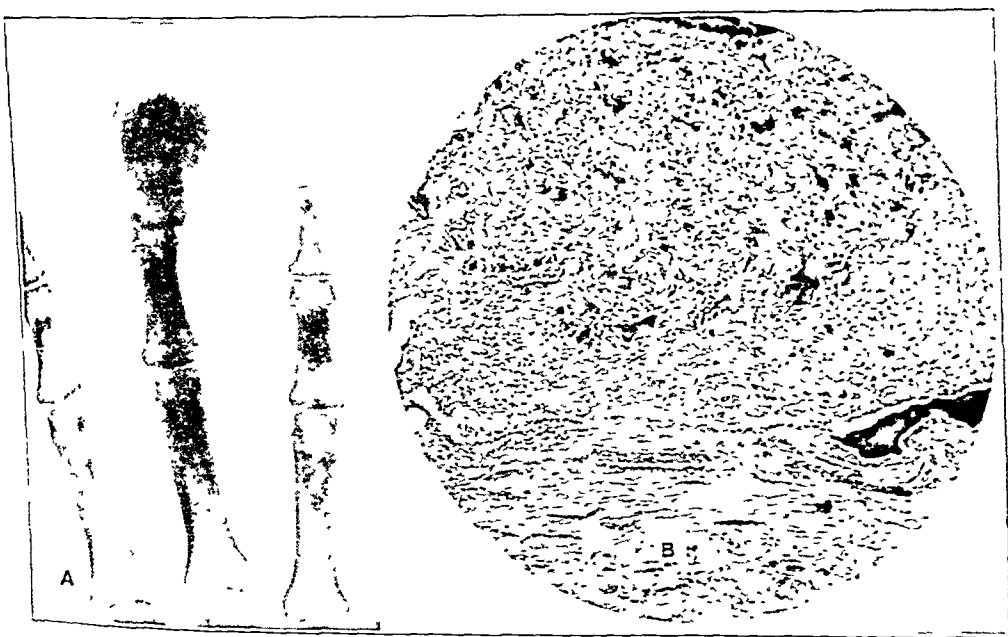


Fig. 27 (nos. 26953 and 17536).—The x-ray picture, *A*, shows a giant cell tumor of the terminal phalanx of the midfinger. There is involvement of both shaft and epiphysis in this small bone, and the tumor has perforated at the distal end. The photomicrograph, *B*, shows a giant cell tumor in the phalanx of a toe. Portions of trabeculae of cancellous bone are undergoing absorption, while the proliferation of fibroblasts in other areas shows a healing reaction.

approximation (fig. 30). Extension is not due to increased virulence of the tumor, as some pathologists claim who consider the spindle cell variant of the giant cell tumor a malignant form of this lesion (Ewing⁷).

From these studies the locality of the bone affected is seen to be an essential and determining factor in the pathologic process of giant cell tumor and the bone cyst. The epiphysis with its less active periosteum and thinner cortex allows the bone destructive giant cell tumor to

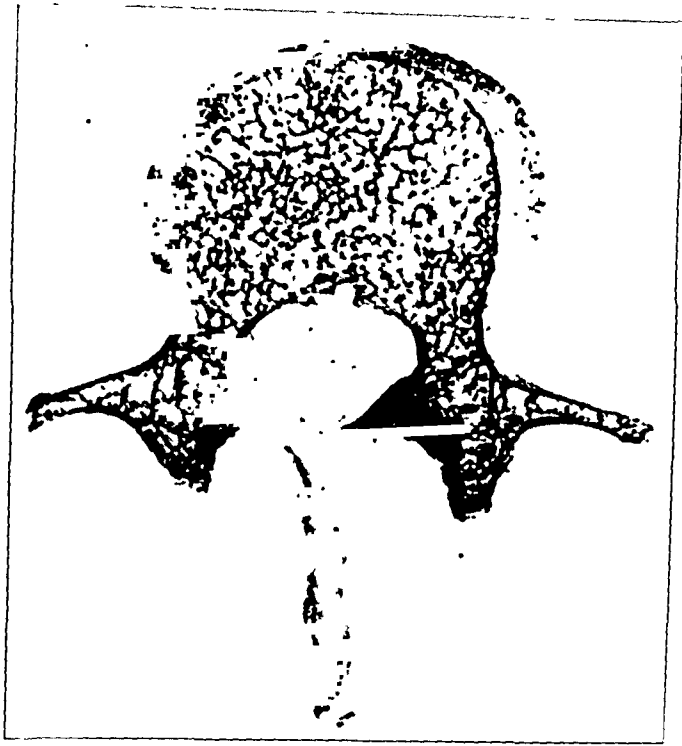


Fig. 28 (after Triepel-Breslau: Anat. Hefte 25:209, 1904).—Cross-section of a lumbar vertebra showing the relation of cancellous to compact bone. As is explained in the text, the most frequent site of giant cell tumors is in the region of the laminae in the body, in the transverse process or in the lamina itself. This brings the tumor into contact with compact bone at an early stage.



Fig. 29 (no. 38530).—Giant cell tumor of a vertebra. The giant cells are embedded in a stroma in which there are many spindle cells.

progress, while the thicker and more resistant cortex of the metaphysis, with its vascular subperiosteal layer promotes healing and makes for an arrested lesion, the bone cyst.

There is another factor of great importance, however, namely age. Bone growth and a bone cell with great proliferating potentialities are characteristic of youth. This power to heal a bone destructive lesion in the early years of life accounts for the fact that the arrested lesion, the bone cyst, is three times more frequent before the age of 20 than the



Fig 30 (no 24682) —Gross specimen showing the involvement of the third and fourth metacarpals by giant cell tumor. There is extension of the bone destructive process to several bones

unhealed giant cell tumor (fig. 31). In fact, although several cases of bone cysts are recorded in this series in the epiphysis in patients under 5 years of age, giant cell lesions in any locality were not observed in patients under that age. The reason for this is that the vascular subperiosteal layer of the epiphysis does not begin to atrophy until after the age of about 3, and hence giant cell lesions arising in the epiphyses will be transformed into bone cysts at these earlier ages by the active periosteum

Figure 31 emphasizes how the age period influences the physiologic factors underlying the differences between giant cell tumor and bone cyst. In this chart it will be seen that giant cell tumors do not occur until after the age of 5 when the periosteum of the epiphysis has lost much of its reparative powers. The healed bone cyst is the predominant lesion during the active growth period when the regenerative power of bone is at its height. To state it briefly, within certain age limits, as the healing powers of bone decline the frequency of the bone cyst decreases, while the frequency of the giant cell tumor increases.

Multiple Giant Cell Tumor and Multiple Osteitis Fibrosa.—A perusal of the contributions to this subject shows that a clinical and

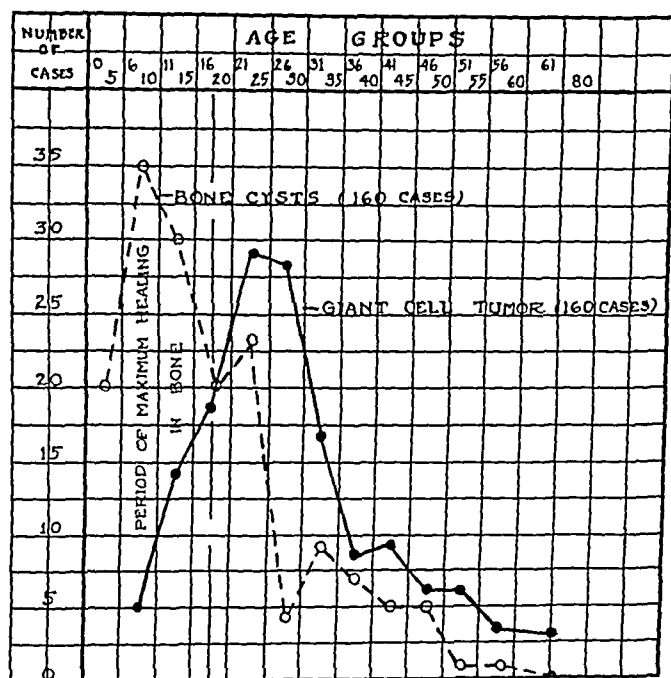


Fig. 31.—The age incidence of giant cell tumor compared with that of bone cysts. Within certain age limits (from 10 to 25) as the healing powers of bone decline, the frequency of bone cysts decreases while that of giant cell tumors increases.

pathologic overlap has long been recognized in this group of multiple tumors between bone cyst and giant cell tumors.^{24a} Morton,¹⁹ in reviewing the literature of multiple bone cysts, divides the lesions into group 1 without giant cell sarcoma and group 2 with giant cell sarcoma. In a similar manner, Alexander and Crawford²⁵ divide multiple giant cell

24a. Both Henderson (Minn. Med. **11**:542, 1928) and Meyerding (J. A. M. A. **83**:1323 (Oct. 25) 1924) recognized a relationship between these two tumors in their reports on solitary giant cell tumors.

25. Alexander, E. G., and Crawford, W. H.: Multiple Giant Cell Tumors, Ann. Surg. **86**:362 (Sept.) 1927.

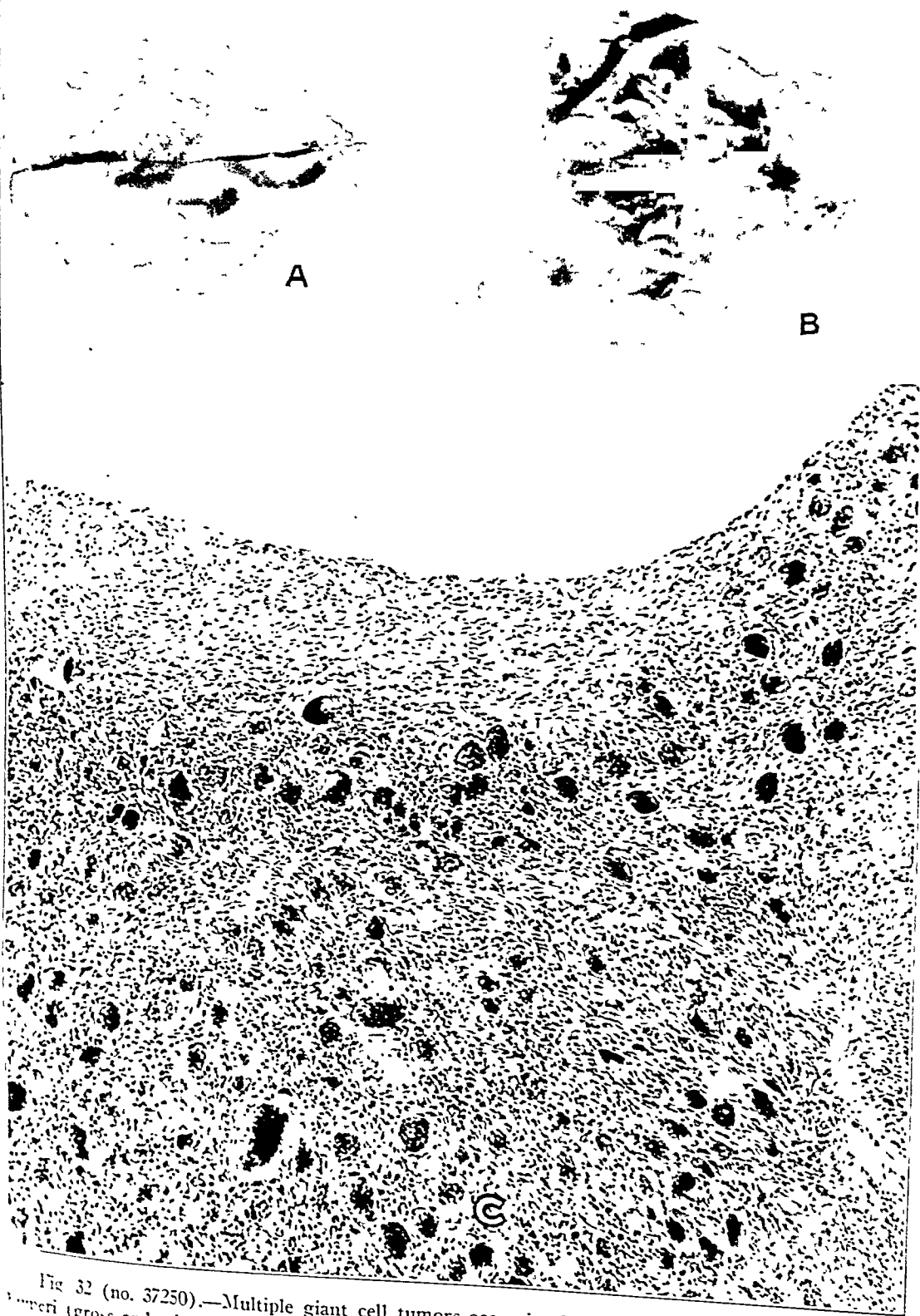


Fig 32 (no. 37250).—Multiple giant cell tumors occurring in the tibia, radius, antrum and both maxillari (gross and microscopic specimens from the same case). *A* and *B* are gross specimens showing the polycystic structure of the tumor; *C* is a photomicrograph showing the numerous large multinucleated giant cells occurring in a cyst wall.

tumors into two groups, those without and those with associated fibrocystic osteitis.

A review of our series of cases (table 8) emphasizes that in females past the age of puberty the condition predominates and that the males affected are usually under 12 and in these patients the condition is frequently associated with other juvenile diseases such as rickets, congenital syphilis, osteogenesis imperfecta and fragilitas ossium. Thus at the beginning of this discussion, it is important to realize that in cases of either multiple giant cell tumors or multiple bone cysts, there is frequently an associated disease, such as is not found in the single bone cysts and local giant cell tumors. Silver¹⁵ implied this when he excluded from consideration in his article cysts occurring in seven different groups of associated diseases. This fact of a complicating disease, however, is not sufficiently emphasized in the reports on this group of tumors, and it must be borne in mind in the following discussion.

Multiple Giant Cell Tumor.—Many important features of the multiple giant cell tumor are illustrated in the following case (path. no. 37250, figs. 32 *A*, *B* and *C* and 33). The patient observed in 1922, was a white woman, aged 21, and the condition was of nine years' duration. The patient was well in 1928. The lesions were in the right tibia, the left radius and both humeri, all occurring just on the diaphyseal side of the epiphyseal line. In addition to this there was a tumor in the left antrum. The specimens illustrated were from the right tibia. In the gross the tumor was polycystic, and under the microscope even smaller cystic areas were present in large numbers. Giant cells predominated in the tissue about the cyst wall, and among these giant cells were numerous round cells. Elsewhere the stroma was composed of spindle cells and fibroblasts and further out there were islands of new bone and typical osteitis fibrosa. There was much hemorrhage in the tissue, and some small cysts were occupied by blood.

There were too many giant cells in the sections for the tumors to be classed as simple cysts. Similarly, we have never observed a case of typical bone cyst in the upper jaw. Yet, the tumors in the long bones are all on the shaft side of the epiphysis, and the patient was only 15 years of age when these lesions first appeared. These two facts and the polycystic nature of the tumor favor osteitis fibrosa, and the sections show numerous areas to this tissue. How is a combination of giant cell tumor and bone cyst to be explained in the same case?

Usually, the single bone cyst is an arrested lesion as we have shown, an arrested giant cell tumor. When it is multiple, and particularly when it is polycystic, we have reason to believe that the general rule has been broken and that the lesion has become progressive. In the above case

TABLE 8.—Multiple Giant Cell Tumor and Bone Cyst

Path. No.	Race, Sex, Age	Location	Symptoms	X-Ray	Treatment	Microscopic	Associated Disease	Results
37229	W. M. 12	Upper humerus, upper lower radius, upper fibula, upper femur	Trauma	Cystic expansion	No operation	No note	Osteogenesis imperfect	Well less than 5 years
36482	W. F. 4	Fibula, tibia, os calcis	Deformity 3½ years	Cyst, fracture, bending	Excision	No note	Osteogenesis imperfecta	Deformity still persists
36206	W. M. 3	Skull, femora, sacrum	Meningitis	Areas of absorption	Explored	No note	Rickets	Unimproved
35702	W. F. 16	Humerus, radius	Dysfunction 10 months	Cystic perforation	Curetted	Cysts with areas of giant cells	Not determined	Well less than 5 years
37250	W. F. 21	Humeri, radius, tibia, upper jaw	Tumor 3 years	No note	Curetted	Cysts with areas of osteitis fibrosa and giant cells	Not determined	Well 3 years
33572	W. F. 22	Vertebra, pelvis femur, tibia	Trauma 8 months	No note	Curetted	Cysts with areas of osteitis fibrosa and giant cells	Not determined	Discharged improved
33258	W. M. 31	Tibia, humerus, radius	Trauma 3 years	No note	Curetted	Cysts with areas of osteitis fibrosa and giant cells	Osteomalacia	Unimproved 3 years later
33151	W. M. 18	Fibula, tibia	Trauma 1 month	Cyst with fracture	No note	No note	Not determined	Discharged well
32732	W. F. 5	Tibia, multiple	No note	Cystic bending	Explored	Cysts with areas of giant cells	Rickets	Discharged improved
31880	W. F. 25	Fibula, tibia, femur	Fracture 3½ years	Cystic bending	No note	Cysts with areas of osteitis fibrosa	Osteogenesis imperfecta	Discharged improved
30316	W. F. 52	Scapula, sacrum, humerus	Trauma 2 years	No note	No operation, x-ray	No note	Not determined	Well 7 years
29810	W. F. 14	Radius, ulna, femur, tibia, fibula	Deformity 7 years	Cystic with rarefaction	No note	No note	Rickets	Discharged improved
28016	W. F. 23	Jaws, pelvis	Tumor 7 months	No note	Curetted	Cysts with areas of osteitis fibrosa and giant cells	Syphilis, congenital	Discharged improved
28071	W. F. 15	Femora, tibia	Deformity 12 years	Cystic bending	Curetted	Cysts with areas of osteitis fibrosa and giant cells	Osteogenesis imperfecta	Discharged improved
20785	W. F. 15	Humerus, hum., ribs	Fracture 3 years	Shaft of humerus destroyed	No note	No note	No note	Well 7 years
25833	W. F. 41	Tibia, hum., femur	Fracture	No note	Resected	Cysts with areas of osteitis fibrosa and giant cells	Osteomalacia	Died of other causes
25801	W. F. 33	Tibia, patella, radius, ulna, humerus	Tumor 6 months	No note	Curetted	Cysts with areas of osteitis fibrosa and giant cells	Multiple perforations	Discharged improved
25800	W. F. 55	Humerus, tibia	Pain	Cystic bending of spine	Excision	No note	Osteomalacia	Discharged improved
25217	W. F. 15	Femur, multiple	Pain and deformity 6 years	Bending, rarefaction	Osteotomy	Areas of osteitis fibrosa	Fragilitas ossium	Recurrence
10523	W. F. 21	Radius, humerus	Pain 2 years	Cystic, encapsulated	Curetted	No note	Undetermined	Well 29 years

the age of onset and the location of the tumors in the metaphysis of the long bones would seem to indicate that had this tumor become arrested, it would have been a typical bone cyst. Instead it had become progressive, showed multiple bone involvement, polycystic structure and a predominance of giant cells, the expected explanation for this failure to be arrested being that there was an associated disease in the skeleton that prevented the usual protective overgrowth of fibro-ostosis from taking place.^{25a} When we review all the multiple cases in the literature, and those in our collection, we are impressed with two facts, that the patients are either females at the age during which osteomalacia occurs or males and young girls at the age in which juvenile bone diseases are common. The associated skeletal diseases vary, but some complicating factor is usually present (fig. 34, *A* and *B*) such as osteogenesis imperfecta, rickets, congenital syphilis, fragilitas ossium and osteomalacia.

From the facts already mentioned, the conclusions follow that most multiple giant cell tumors would, without a complicating factor, develop clinically into a bone cyst and that their failure to become so arrested and the persistence of giant cell areas in them indicate a progressive lesion. The giant cells present indicate the more primitive and original structures of these lesions, and ordinarily they disappear from the healing solitary bone cysts by the time that the lesion comes under observation. These multiple giant cell tumors, therefore, throw considerable light on the earlier stages of osteitis fibrosa.

Multiple Bone Cysts.—A review of multiple bone cysts in the literature and in our own series emphasizes the fact that the lesions described under this head represent a conglomeration of pathologic entities.

25a Although in this case we had at our disposal only the history, x-rays and microscopic material, and although we were unable to verify the conclusion by metabolic studies, the fundamental conception advanced here has been recently confirmed by evidence placed at our disposal through the courtesy of Dr. R. M. Wilder of the Medical Division of the Mayo Clinic. The case, that of a white woman, aged 32, studied by him over a period of four years (to be reported in *Endocrinology*) duplicates in its essential clinical features the one already outlined, and in addition shows abnormal calcium and phosphorus values in the blood serum which ultimately proved dependent on a hyperparathyroidism associated with a benign adenomatous tumor of the parathyroid gland. Giant cell tumors occurred in the lower part of the femur, the upper jaw and at the site of the right lower bicuspid (epulis). The serum calcium was elevated to 11.4 mg. per hundred cubic centimeters, and the phosphorus lowered to 1.4 mg. per hundred cubic centimeters. As a result of this removal of lime salts from the bones, the pelvis showed rarefaction and distortion similar to osteomalacia and the skull and spine areas of absorption. Improvement followed removal of the parathyroid tumor, a diet high in vitamins and ultraviolet light therapy. The serum calcium had returned to 8.3 mg. per hundred cubic centimeters and the phosphorus to 1.8 mg. per hundred cubic centimeters when the patient was last examined in April, 1929.



Fig 33 (no 37250) —Low magnification of the cyst shown partially in figure 32 C. The numerous black dots in the tissue are seen to be giant cells under higher magnification. The broken septum dangling from the roof of the cyst shows that the fusion of two minute cysts has occurred.

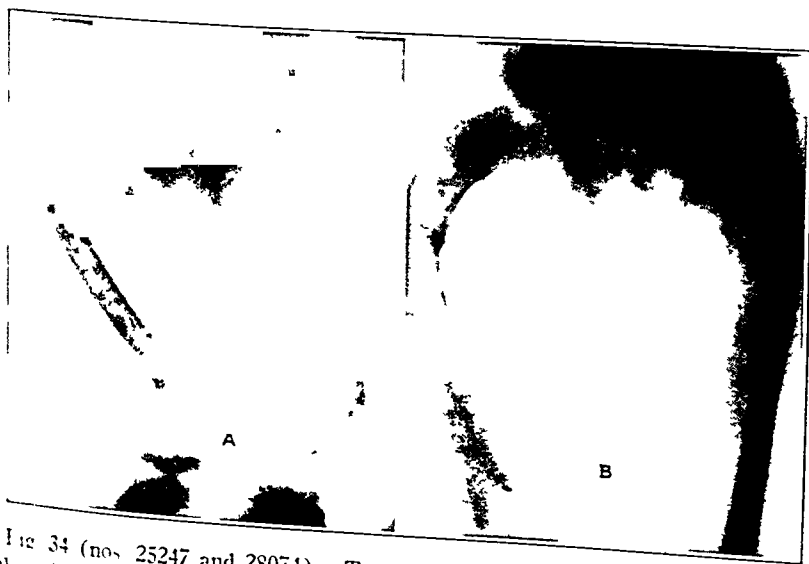


Fig 34 (nos 25247 and 28074) —Two cases showing associated skeletal disease with multiple bone cysts and multiple giant cell areas. The bending of the bones and the pathologic fractures are associated with fragilitas ossium (A) and osteoporosis imperfecta (B).

When selected on a microscopic basis, these lesions show under the microscope a predominance of osteitis fibrosa, fewer, but some giant cells, and less of the polycystic structure. Clinically, this group is to be distinguished from multiple giant cell tumors by the higher age limits and the longer duration of the symptoms. This is what would be expected if multiple bone cysts represented a later stage in the same pathologic process as multiple giant cell tumors. When outspoken cases of Paget's osteitis deformans, osteomalacia, osteoarthritis and similar diseases are excluded, all the evidence is found to support this view. When the cysts were large and the tissue sparse in giant cells, we found the average age of the patients to be higher and the duration of the symptoms to be longer (table 8). Ultimate healing without surgical intervention occurs in multiple bone cysts, the process responsible for the multiplicity of the lesion apparently subsiding, although the cysts themselves may remain many years as latent lesions. In such cases it will not be possible to find an associated disease when these lesions come under observation at a late date.

In passing it is well to note here certain observations made in this group of multiple bone tumors. In the majority of the twenty cases in this series studied in this laboratory the urine was examined for Bence Jones bodies. In all cases the results of the examination were negative, an interesting diagnostic point in view of the frequency of Bence Jones bodies in the urine of patients with multiple myeloma (65 per cent), and the association of these bodies with other multiple bone tumors (Geschickter and Copeland ²⁶).

THE NATURE OF THE GIANT CELL

It has been pointed out that the giant cell tumor under the microscope shows a typical structure characterized by many large giant cells embedded in a round cell stroma. The spindle cell variant of this histologic picture and indeed, the microscopic structure of osteitis fibrosa and its variants were shown to be due to a healing reaction or fibro-ostosis in most instances superimposed on the original giant cell picture. In this way and also by pointing out transitional lesions, it was shown that these various forms of disease of the bone in all probability originate from a single underlying pathologic process characterized histologically by the proliferation of giant cells. A fundamental importance, therefore, attaches to the elucidation of the nature of the giant cell and the causes for its proliferation.

In contrast to the bone formative tissue of fibro-ostosis, giant cell areas in the skeleton are associated with bone destruction. This is well

26. Geschickter, C. F., and Copeland, M. M.: Multiple Myeloma, *Arch. Surg.* 16:807 (April) 1928.

illustrated by figure 35 which shows a bone spicule lying at the margin of a giant cell tumor occurring in the lower epiphysis of the femur. At one end, the spicule is enlarged and club-shaped and in contact with it are numerous osteoblasts applied to its surface. Surrounding this enlarged end, beyond the osteoblasts, are numerous spindle cells and fibroblasts. At this end there is little doubt that new bone formation is taking place. At the other end the spicule is narrower, and the margins are frayed and worm eaten in appearance. Near at hand are giant cells



Fig. 35 (no. 3623).—A bone spicule from the margin of a giant cell tumor in the lower end of the femur. At the large end of the spicule, osteoblasts embedded in fibrous tissue are laying down new bone. At the small tumor margin of the spicule, the frayed and worn edges indicate bone destruction. Both the bone destructive nature of giant cell tumor and the healing reaction of fibro-ostosis are illustrated by this section.

embedded in a round cell stroma. The histologic picture at this end of the spicule is that of typical giant cell tumor, and it is plainly evident that bone destruction is occurring here.

Varieties.—The question arises whether the giant cells in the tumor are responsible for this bone destruction and if the tumor process repre-

sents a proliferation of osteoclasts as pointed out by Stewart of Leeds.⁴ Much work has been expended in an endeavor to determine whether the giant cell erodes bone. The question has not been conclusively settled, although a well defined distinction has been drawn between giant cells of the hemopoietic series, giant cells in malignant tumors with rapid mitoses, and foreign body giant cells. The so-called osteoclast or giant cell of the epulis type found in giant cell tumor is undoubtedly related to the foreign body type. It represents a formation of cells characteristic of a phagocytic process, and as Lewis²⁷ has shown, these larger elements are formed by the fusion of smaller cells, with occasionally a further multiplication of nuclei by mitotic division. Giant cells of this phagocytic type are found when agar-agar is introduced into muscle, about foreign bodies introduced into wounds, about gummas and tubercles, epithelial pearls in squamous cell carcinoma and about necrotic fibrous tissue in other tumors. The presence of these cells in such a miscellaneous group of lesions is probably to be explained on a basis of a chemotaxis to a collagen-like substance present in all of these conditions. It is important to recall in this connection that Leriche and Policard^{22a} have recently shown that a collagenous matrix is fundamental to the formation of all bony substances.

But though related to the foreign body type in formation and phagocytic nature, the giant cell of giant cell tumor with its typical retinue of round cells is by no means to be confused with the foreign body giant cell embedded in granulation tissue. No particular histologic training is necessary to distinguish between these two types of tissue, and the current tendency to regard giant cell tissue everywhere as granulation tissue and to interpret all tumors of this form on such a basis is unjustifiable despite the contentions of Mallory,²⁸ Konjetzny²⁰ and many others.

Histologically the giant cell in granulation tissue is a smaller cell, with fewer nuclei, peripherally rather than centrally placed. The surrounding round cells are leukocytes of various types and are relatively small. The giant cells although clumped rarely average as many as 10 or 15 cells to a low powered field. In typical giant cell tumor tissue the giant cells are larger, have more nuclei (from 15 to 200) centrally placed and average over 30 to the low powered field. The accompanying round cells are not of the infectious leukocytic type but are larger, more uniform in size and structure, and their nuclei correspond in morphology to the nuclei of the giant cells.

27. Lewis, W. H.: Mononuclear Blood Cells, The Harvey Lectures, 1925-1926, series 21, p. 83.

28. Mallory, F. B.: Giant Cell Sarcoma, J. M. Research **74**:463, 1911.

Fundamentally there is a difference, and while recognizing the giant cell of the epulis type as related to the foreign body series, we view it as a specialized form and propose to demonstrate the osteoclastic nature of all giant cell tumors and their inherent relation to bone even when occurring in the soft parts.

Such a view of the osteoclastic giant cells interprets them as phagocytic elements which exhibit the property of giant cell formation when bone or calcified cartilage is being resorbed. The question of whether the giant cells directly or indirectly, mechanically or chemically are accomplishing the bone destruction is irrelevant to this discussion. Suffice it to say, that they are an early manifestation rather than an end-product of bone destruction as claimed by Arey,²⁹ and they may be taken as an index that the process is active, since when this type of tissue proliferates the process increases. Embryologic studies emphasize this point.

The Relation of the Histogenesis of Intracartilaginous Ossification to Giant Cell Tumor.—Although works on embryology since 1890 (Quain³⁰) give the histogenesis of the long bones in some detail, the importance of this process for giant cell tumor made a reconsideration of the whole process essential. For this purpose we were fortunate in having the privilege of studying a most valuable collection of human embryos in the Carnegie Institute of embryology placed at our disposal through the courtesy of Professor Streeter, director of the institute.

In the long bones, the process of osteogenesis is similar in both the shaft and the epiphysis, the two being formed by intracartilaginous ossification. There are usually three centers of ossification, one for the diaphysis and one for each epiphysis. The center of ossification of the shaft develops first, new bone extending in two directions toward each metaphysis. The two epiphyseal centers develop much later (fig. 36). Hence, the areas in which new bone formation persists in the child and the young adult are in the metaphysis of the bones on the shaft side of the epiphyseal line and in the epiphysis. As we have seen, these persisting centers of ossification are the sites of the lesions of bone cysts and giant cell tumor. The histologic processes going on in these regions or centers explain how these growths arise.

The new bone is preformed in cartilage and later replaced by permanent bone. This process may be said to take place by transformations occurring in three stages: (1) the calcification of cartilage to form primary areolae; (2) the invasion and resorption of the areolae and

²⁹ Arey, L. B.: Origin and Fate of Osteoclasts, *Am. J. Anat.* **26**:315, 1919-1920

³⁰ Schafer, E. A., and Thane, G. D.: Quain's Elements of Anatomy, ed. 10, 1911, vol. 1, part 2, pp. 268-284.

their walls; (3) the laying down of permanent perichondral bone. Both longitudinal and transverse sections are necessary to a clear conception of these three stages, and both are illustrated here (figs. 36 to 41). In the longitudinal sections the ends of the bone are still primitive cartilage. Toward the center of the shaft, the cartilage cells line up in rows, enlarge and secrete an increased hyalin matrix which becomes calcified to form a honey-combed arrangement. The cartilage cells within these calcified



Fig. 36 (no. 40936).—The femur of a monkey fetus at term. The photograph illustrates the persistence of cartilage in the epiphysis and the formation of new bone in the metaphysis. The marrow cavity is not yet fully formed.

compartments next shrivel and atrophy, their nutrition being cut off by the calcified walls which form the primary areolae. All this occurs in the regions that are the future medullary cavity. In the subperichondral region (what is to be subperiosteal) along the margins of the shaft, osteoid tissue is being laid down by the perichondrium. In the next stage, this perichondral osteoid tissue is perforated by blood vessels that proceed inwardly to the primary areolae (fig. 40 *A* and *B*).

This stage in which the calcified areolae are invaded by blood vessels and resorbed is the most significant phase for the understanding of giant cell tumor and is best seen in cross-sections taken from the long bones of young human embryos. It is just this phase that is most poorly described in the textbooks, and the cross-sections illustrated here are usually omitted. In the transverse sections it will be seen that the primary areolae are invaded and resorbed by buds of tissue proceeding from the outlying mesenchyme surrounding the perichondral bone. The manner in which these buds perforate the perichondral bone, invade the calcified areolae and absorb them is most important. Mesenchymal cells

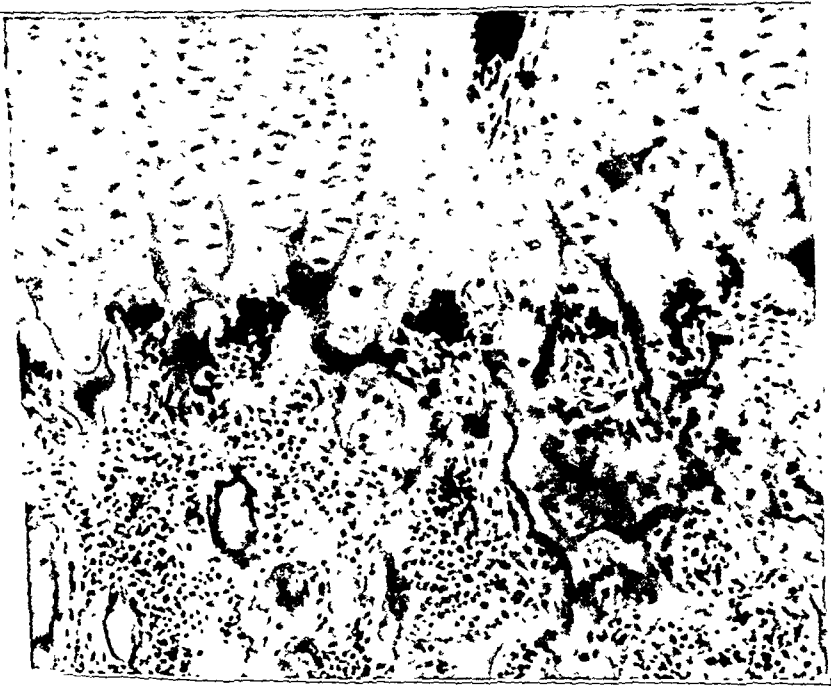


Fig. 37 (no. 40936).—Photomicrograph of the epiphyseal line of the femur shown in figure 36. Cartilage has calcified to form the primary areolae. Giant cells or osteoclasts are eating their way into the calcified cartilage followed by small vessels, preliminary to the formation of permanent bone. Cells of the newly formed marrow cavity are seen at the bottom of the picture.

concentrate, their nuclei darken and the cells agglutinate to form giant cells or osteoclasts. These giant cells are first to perforate the perichondral bone (fig. 41) and the first to force entrance into the compartments of the calcified areolae (figs. 37 and 38). In their wake come newly formed capillaries, osteoblasts and other mesenchymal elements. When the stage of resorption of calcified cartilage is at its height, and the medullary cavity is being formed, a cross-section of a young bone in an embryo of from 90 to 100 mm., taken from this region, will show a

veritable giant cell tumor. The cavity of the bone will be filled with giant cells, round cells, small blood vessels, hemorrhage and osteoblasts. Later the osteoblasts persist near the margin of the medullary cavity to aid in the formation of cancellous and then compact bone, while the marrow cavity itself becomes filled with young bone marrow elements.

These embryologic studies emphasize the association of the giant cells with the perforation of new perichondral bone and the resorption of calcified cartilage. The specimens show clearly that the giant cell

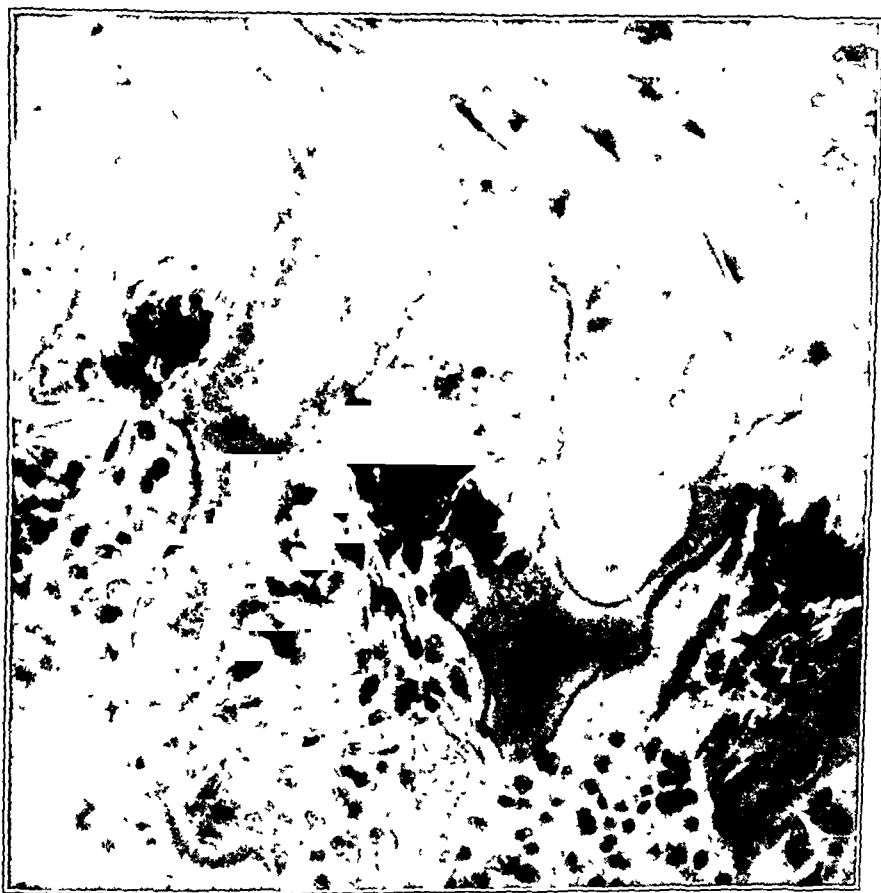


Fig. 38 (no. 40936) —Higher magnification of the same area shown in figure 37. Three primary areolae formed by calcified cartilage with a portion of two others are shown in the photomicrograph. One areola is still intact, and in it two degenerating nuclei of cartilage cells are seen. In the other areolae giant cells are seen forcing their entrance through calcified cartilage. Note that the nuclei of the giant cells are entirely different in morphology from those of the degenerated cartilage cells, and that they outnumber the cells in the calcified area. This disproves the statement of Arey that giant cells are rarely seen when calcified cartilage is undergoing resorption and that the giant cells are formed as a by-product of degenerated dissolving bone by the agglutination of the nuclei of old bone cells.

proceeds inwardly from outside of the shaft of the bone and that these multinucleated elements may arise in the primitive periosteal tissue. It is not necessary to presume that they arise from the marrow reticulum as many histologists believe (Maximow³¹) nor that they are derived from the endothelium of capillaries. The only distinct evidence is in favor of the view that they are formed from primitive mesenchyme and that such mesenchyme exists periosteally.

Giant cell formation, therefore, marks the beginning of bone perforation in the embryo, and in the wake of these cells new blood vessels and osteoblasts follow. Over and over again in both giant cell tumor and osteitis fibrosa, particularly of the polycystic variety, we have observed giant cells on the outward borders of new blood vessels and vascular spaces (figs. 5, 45 and 57) showing that the giant cells in these lesions retain the same histologic function as the osteoclasts seen in human and other mammalian embryos.^{31a}

Other points of interest in the embryologic processes of bone are the formation of perichondral osteoid tissue directly from the mesenchymal osteoblasts without the medium of cartilage which parallels exactly the bone formation described in this paper as fibro-ostosis, and the resemblance of calcified cartilage in the embryo to analogous tissue seen in osteogenic sarcoma.

Turning now to the consideration of giant cell tumors, the location of these lesions (and also the healing form of bone cysts) at the sites and at the ages when intracartilaginous bone is being formed relates them to this process. More specifically and convincingly the bone destructive character of these lesions and the prevalence of giant cells or osteoclasts in them relates them to the process of resorption of temporary bone characterized by the proliferation of osteoclasts or giant cells which has been described in the foregoing review of histogenesis in the long bones. From this we conclude that the giant cell tumor and the related lesion of bone cyst are the result of an abnormal hyperplasia of osteoclasts preceded by a normal stage in which osteoclastic proliferation is taking place as a phase in the histogenesis of intracartilaginous bone. From this point of view, the term progressive osteoclastasia is suggested for the process underlying the giant cell tumor and the term

31. Maximow, A.: Untersuchungen über Blut und Bindegewebe, Arch. f. mikr. Anat. 76:1, 1910.

31a. That this same histologic function of the osteoclasts as forerunners of the vascularization and resorption of temporary calcified structures holds for repair processes and even for foreign bodies is shown by the experiments of Pollock and others on the viability of transplanted bone (Arch. Surg. 18:607 [Feb.] 1929). Here in experimental bone transplants it was found that giant cells attacked the transplanted bone preliminary to its vascularization and the formation of new bone.

regressive osteoclastasia for bone cysts. These terms show their relationships one to the other and also to the normal process of osteoclastic proliferation that goes on in the histogenesis of the long bones.

GIANT CELL TUMORS OF THE SKULL

The validity of the hypothesis which relates giant cell tumor to the resorption of temporary bone or calcified cartilage is to be proved by the elucidation and the prediction of the facts in regard to these tumors wherever they are found. So far as giant cell tumors and bone cysts in the long bones are concerned, this conception holds, for by age incidence,

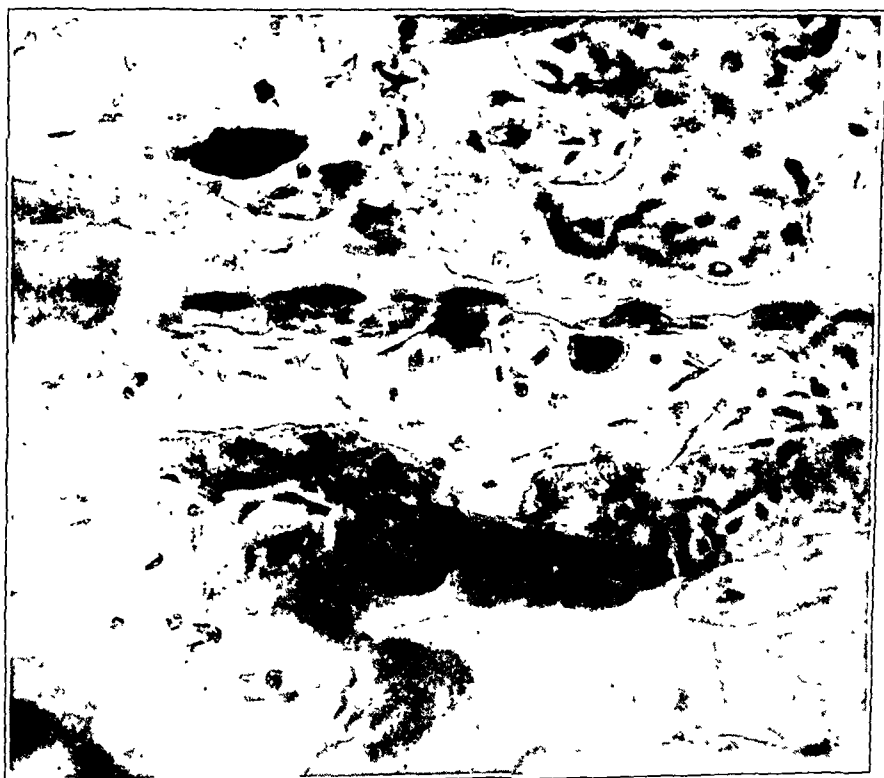


Fig. 39 (no. 40978).—High power field of an epiphysis of a child 11 months old showing calcified cartilage attacked by giant cells. This shows a similar process which is more clearly illustrated in figures 37 and 38.

location and histologic structure these lesions are related to osteogenesis via cartilage. However, tumors of the giant cell variety occurring in the skull, along the alveolar border in the form of the giant cell epulis, and in tendon sheaths and soft parts offer greater difficulties in the establishment of this relationship to the resorption of temporary bone. To predict such a relationship for giant cell tissue in this diversity of lesions is to bring the conception of giant cell tumor thus far advanced to a crucial test. In order to carry out this test these various types of lesions will now be examined in detail.

The Chondrocranium in Relation to Giant Cell Tumors of the Skull.

—If the intimate association of the pathologic changes in giant cell lesions to the resorptive process in cartilaginous bone is a fact, then the bones of the skull and face should furnish valuable evidence to support it. For it is known that certain bones of the cranium—particularly the frontal, parietal and tabular portion of the occipital—which compose



Fig. 40 (no. 40934).—Cross-sections of the humerus of a human embryo of 90 mm. The upper section, *A*, shows the perforation of the perichondral osteoid tissue by mesenchymal elements at numerous points proceeding inwardly from the primitive periosteum. The calcified cartilage is about to undergo resorption by these invading mesenchymal elements. *B* is a section near the region of the mid-shaft of the same bone, showing a more advanced stage in the resorption of calcified cartilage by mesenchymal elements and the formation of the marrow cavity. Note how the subperichondral osteoid tissue has been broken through at different points. (Sections furnished through the courtesy of Dr. Streeter of the Carnegie Institute of Embryology.)

the calvarium are formed from membrane rather than cartilage, as are most of the bones of the face. These bones should be immune to direct involvement by either osteitis fibrosa or giant cell tumor. It is true that they are provided with periosteum and that this tissue retains osteoclastic as well as osteoblastic potentialities, but in such instances, the lesion should be periosteal instead of central and present other peculiarities. A review, therefore, of the exact histology and location of giant cell tumors of the head becomes of special significance.

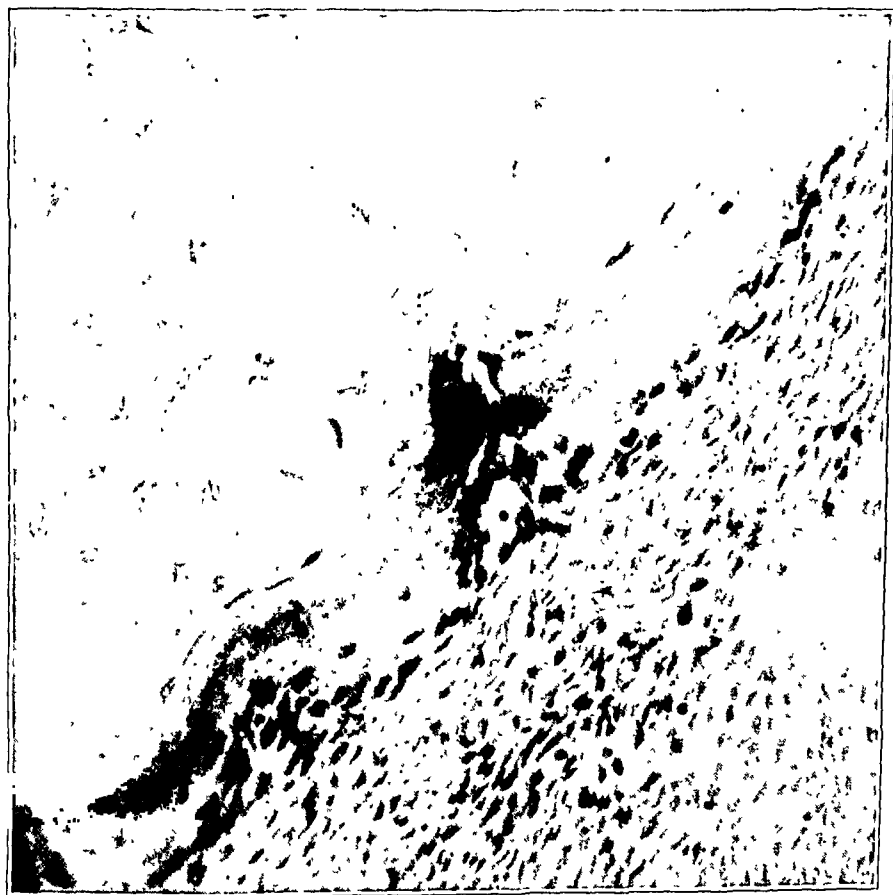


Fig. 41 (no. 40934).—Higher magnification of the section shown in figure 40 A. The photomicrograph illustrates the first step in the resorption of calcified cartilage. A giant cell proceeding from the primitive periosteum is perforating the perichondral osteoid tissue and attacking the primary areola. In its wake is shown a small blood vessel and other mesenchymal elements arising from the primitive periosteum. The picture disproves the assumption by numerous embryologists that the giant cells of an osteoclastic nature are formed from the reticulum in the marrow cavity, for here we see that the giant cell is entering the future marrow cavity from the periosteum outside of the bone.

Excluding the epulis of the alveolar border the records of the surgical pathologic laboratory of the Johns Hopkins Hospital extending over a period of thirty-five years show only twenty-two cases of giant cell

tumor occurring in the head. Bone cysts did not occur in this locality. Two of the giant cell tumors were found in the temporal fossa, six are recorded for the upper jaw and fourteen in the lower jaw. In the purely membranous portion of the calvarium (the frontal and parietal bones), not a single instance of these lesions is recorded (tables 10 and 11). The three sites of the lesions, the temporal fossa, the upper jaw and the mandible, it is true, are in regions of membranous bone. The squamous portion of the temporal bone, the superior maxillae and a large portion of the mandible are formed from membrane. But there are also cartilaginous centers of ossification in the neighborhood of the temporal fossa, the maxilla and the mandible. It becomes necessary.

TABLE 9.—*Relationships of Centers of Ossification of the Chondrocranium**

Chondrocranial Regions	Centers of Ossification	Parts of Adult Skull
Occipital.....	(Basioccipital)	Basilar process of occipital bone Occipital condyles Squamous portion of occipital bone below the superior nuchal line
Sphenoid.....	Basisphenoid..... Presphenoid..... Lingulae..... Alae magnae..... Alae parvae.....	Body of sphenoid bone Body of sphenoid bone Greater part of alae magnae Alae parvae
Periotic capsule.....	Petrous primordium.....	{Petrous portion} {Mastoid portion} of temporal bone
	Nasal septum (mesothmoid)...	{Lamina perpendicularis {Crista galli {Nasal septum (cartilage)
Ethmoid.....	{Paranasals (ectethmoids)..... Cribiform plates..... Inferior conchae..... Sphenoidal conchae.....	{Lateral masses of ethmoid bone Superior conchae Middle conchae Cribiform plates Inferior conchae Sphenoidal conchae

* From Jordan and Kindred: *A Textbook of Embryology*, New York, D. Appleton & Company, 1926.

therefore, to delineate carefully the areas of bone derived from cartilage in the skull and to examine the twenty-two lesions recorded to determine whether their locations coincide with such cartilaginous areas.

Table 9 from Jordan and Kindred³² summarizes the essential points in the histogenesis of the chondrocranium. The same information is duplicated diagrammatically in figure 42. Here the portions of the skull derived from cartilage are represented by areas in black, and in figure 43 the twenty-two lesions occurring in the skull have been plotted according to location. It will be seen at a glance that the giant cell tumors in the lower jaw which is the most frequent site for these tumors of the skull coincide in locality with centers of intracartilaginous ossifica-

32. Jordan, H. E., and Kindred, J. E.: *A Textbook of Embryology*, New York, D. Appleton & Company, 1926.

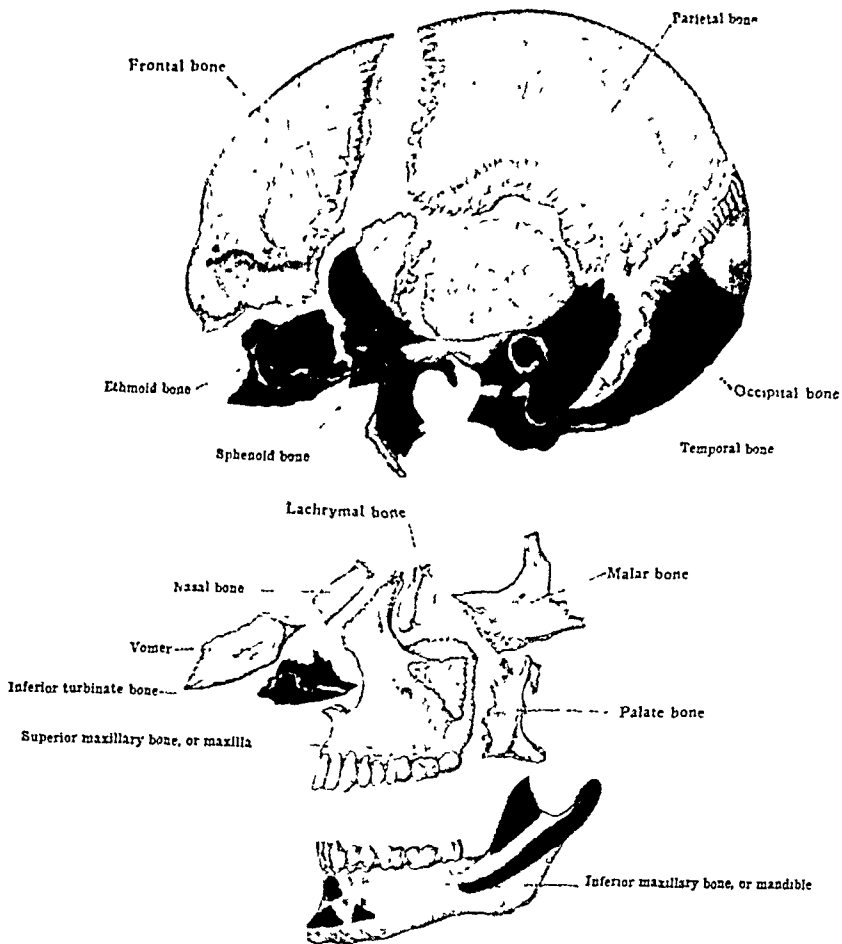


Fig. 42 (after Toldt).—The areas in black show the portions of the adult skull formed from cartilage; see table 9.

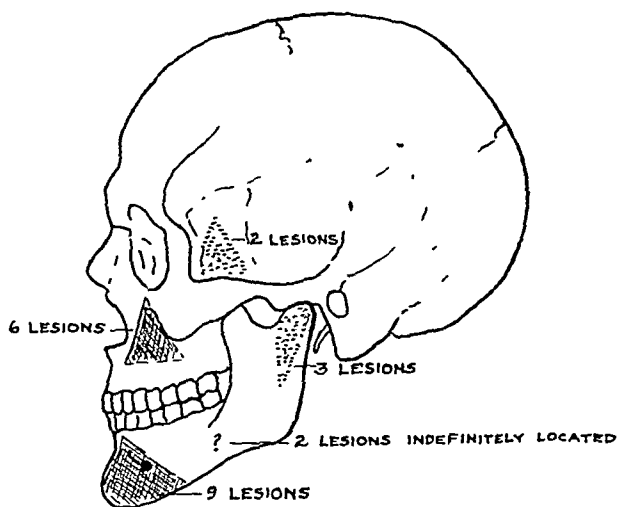


Fig. 43.—Diagram illustrating the location of twenty-two giant cell tumors of the skull. Compare with figure 42. See also tables 10 and 11.

tion for the mandible. The two lesions in the temporal fossa are associated with the wing of the sphenoid (which is derived from cartilage) projecting into this locality. These facts are further substantiated by

TABLE 10—Giant Cell Tumors of the Lower Jaw

Path No	Date	Race, Sex, Age	Location	Symptoms	Operation	Microscopic	Results
42963	9/9/27	W M 13	Mandible at canine	Tumor 1 year	Curetting	Typical giant cell areas	Discharged well
36730	6/9/25	W F 12	Mandible, symphysis	Tumor 6 weeks	Curetting	Typical giant cell areas	Well 2 years
36182	1/7/25	W	Mandible, ramus	Tumor	Resection	Typical giant cell areas	Discharged well
36170	12/9/24	W F 32	Mandible, symphysis	Tumor 1 year	Curetting	Spindle cell variant	Well 7 years
33246	4/10/24	W M 16	Mandible, symphysis	Loose teeth	Curetting	Spindle cell variant	Well 7 years
32991	5/15/23	W F 23	Mandible, ramus	Tumor 3 years	Curetting	Spindle cell variant	Recurred
28405	3/22/23	W F 42	Mandible, symphysis	Tumor 10 months	Curetting	Spindle cell variant	Discharged well
28392	6/21/21	W M 6	Mandible, ramus	Tumor 6 months	Curetting	Spindle cell variant	Discharged well
27281	10/21/20	W F 20	Mandible	Tumor 7 months	Curetting	Spindle cell variant	Well 1 year
27018	11/6/20	W F 41	Mandible, symphysis	Tumor 3 months	Curetting	Spindle cell variant	Well 6 years
13751 ²	1/0/14	W M 11	Mandible	Tumor	Curetting	Spindle cell variant	Well 6 years
7634	10/0/06	W M 10	Mandible, symphysis	Tumor 3 months	Resection	Spindle cell variant	Well 15 years
6277	1903	W F 13	Mandible, symphysis	Tumor	Resection	Spindle cell variant	Well 17 years
2934	4/14/00	W F 21	Mandible, symphysis	Tumor 10 months	Resection with glands	Spindle cell variant	Well 21 years

TABLE 11—Giant Cell Tumors of the Skull and Upper Jaw

Path No	Date	Race, Sex, Age	Location	Symptoms	Operation	Microscopic	Results
37014	2/1/23	W F 52	Body of sphenoid	Pain 3 years	Excision	Typical giant cell	Hemiplegia 4 years later
14332 ²	5/0/03	W F 14	Temporal fossa	Pain 18 months	Excision	None	Well 20 years
43109	2/21/20	W M 9	Antrum, right	Tumor 6 months	Curetting	Spindle cell variant	Discharged well
7240*	11/2/25	W F 21	Antrum, left	Tumor 7 months	Explored	Giant cell areas	Well 1 year
7708	9/22/25	W F 13	Antrum, right	Tumor 2 months	Curetting	Spindle cell variant	Discharged well
2828*	7/20/07	W F 18	Antrum and orbit	Tumor	Partial curetting	Spindle cell variant	Well 13 years
2846*	8/0/21	W F 25	Antrum	Tumor 7 months	Curetting	Spindle cell variant	Draining sinus
2829*	8/21/11	W F 9	Antrum, left	Tumor 3 weeks	Resection	Spindle cell variant	Well 5 years

* Multiple tumor in other bones

the data in table 10. In this table it is seen that in the mandible most of the giant cell tumors occur at the symphysis where Meckel's cartilage participates in the formation of this bone. The others are located at the ramus where there is a separate center for cartilaginous ossification. Table 11 also correlates the origin of the lesions in the temporal fossa

with cartilaginous centers in the sphenoid bone projecting into this region. The only discrepancy is apparently in regard to the six lesions of the upper jaw. In table 11, however, it is seen that all of these tumors found their way either into the antrum or into the orbital fossa. The ethmoid bone which is entirely derived from cartilage is in relation to both of these cavities as is shown in figure 44 *A* and *B*.

The fact that neither bone cysts nor giant cell tumors can be found in the portions of the skull which are entirely of membranous origin and the fact that they always occur at least in proximity to areas of cartilaginous ossification is more than suggestive if not convincing. Such evidence is worthy of scrutiny in more detail.

Giant Cell Tumors of the Temporal Fossa.—The history of two such cases are on file in the surgical pathologic laboratory. Only the

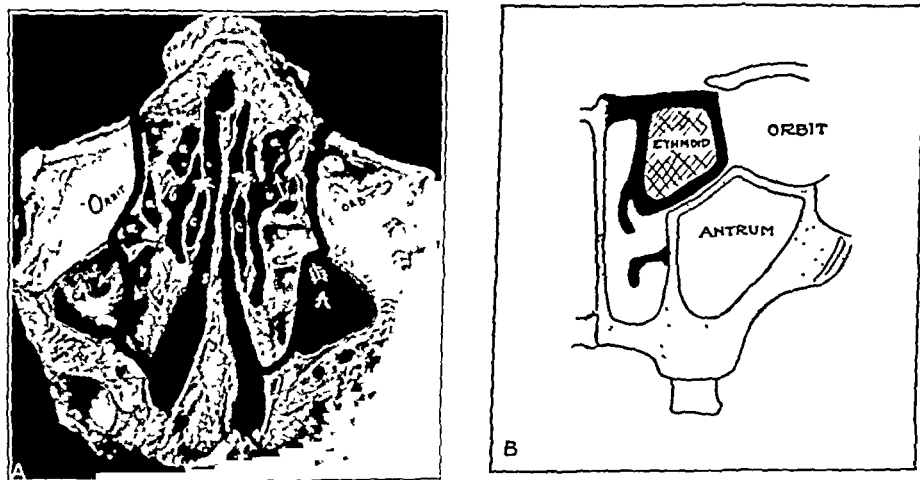


Fig. 44 (from Lothrop: *Ann. Surg.* **38**:233, 1903).—*A*, horizontal section above the level of the ostium maxillare. Within the figure, *A* indicates the antrum with arrows indicating the position of the ostium maxillare and lying in the infundibulum; *U*, uncinate process; the cavity just external to the letter is the infundibulum; *a, a*, anterior ethmoid cells; *p*, posterior ethmoid cells; *s*, septum nasi; *O*, orbital fossa; *m. t.*, middle turbinates. The posterior half of each turbinate is horizontal; the anterior half is vertical, and each instance the turbinate contains a cell (*c*). The dark space external to these turbinates is the middle meatus, and the long, dark area internal to the turbinates divided by the septum is the general cavity of the nasal fossa. The anatomic specimen shows the ethmoid bone which is formed from cartilage outlined in black and demonstrates the relation of this bone to the antrum and orbit. *B* (after Frazer: *The Anatomy of the Human Skeleton*, p. 245) is a diagram illustrating the position of the labyrinth of the ethmoid in relation to the orbit and antrum.

first is reviewed here because the records of it are complete in every detail. The patient was a white woman, aged 52, with pain near the right ear of three years' duration, and dizziness for six months. Exami-

nation showed deafness in the right ear, ataxia with deviation to the right, swelling over the right temporal region and a negative cerebrospinal fluid. At the operation the tumor was partially removed by excision. There was extension about the base of the pons which was deemed inoperable. Four years after operation the patient had a fully developed hemiplegia due to the continued growth of the tumor left behind. Under the microscope sections of the tumor showed a typical giant cell lesion

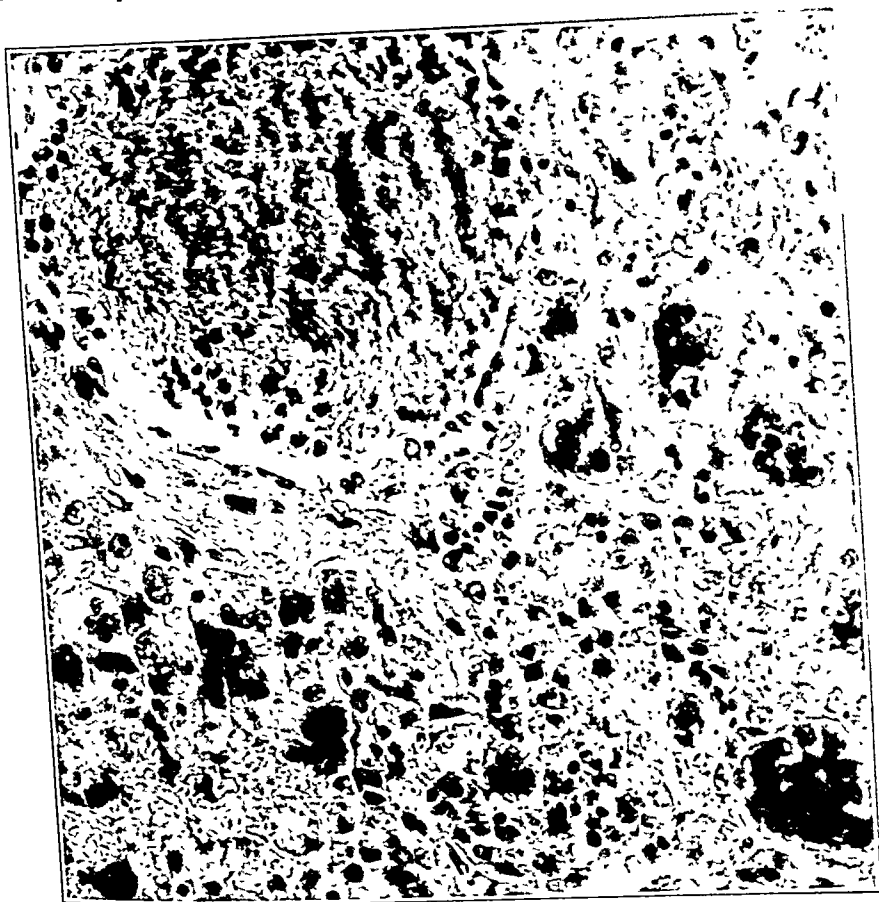


Fig. 45 (no. 37914).—A giant cell tumor arising from the body of the sphenoid and presenting in the temporal fossa. Attention is directed to the relation of the giant cells to the newly formed blood cavity.

(fig. 45). Careful inquiry into the operative notes shows that the origin of the lesion was from the posterior body of the sphenoid extending into the great wing around the carotid groove. This definitely relates the tumor to a center of cartilaginous ossification.

Giant Cell Tumors of the Upper Jaw.—All six of these tumors of the upper jaw presented into the antrum and one involved the floor of the orbit as well. Two of the six were multiple lesions occurring also

in other bones as will be seen from table 11. Tissue taken from the antrum was examined microscopically in every case except in the two multiple lesions, where tissue was taken from other bones (in one case the lower jaw, in the other the tibia), the histologic nature of the antrum tumors being inferred. In every case, the tissue was graded as a spindle cell variant of giant cell tumor, microscopically. In all of them careful search, where the records were sufficiently detailed, related these lesions to the ethmoid bone which would account for their origin from a cartilaginous center and the tendency of these tumors to present in the antrum or the floor of the orbit (fig. 44 *A* and *B*). Interestingly enough the illustration from Nélaton's work on giant cell tumors published in 1860 shows a lesion of the upper jaw, and the picture demonstrates clearly the relation of the tumor to the ethmoid bone and the inferior nasal concha. We have reproduced this illustration in this article (fig. 46).

Giant Cell Tumors of the Lower Jaw.—Lesions in the mandible show a preference for the area between the symphysis and mental foramen. Occasionally one is located at the ramus. This unique distribution of these tumors is readily comprehended when the process is related to intracartilaginous ossification.

Unfortunately little regard has been paid in either the literature or the clinics to the exact location of giant cell tumors in the head. All the available cases studied by us support the belief that the origin of the pathologic process involved is at the sites of bone formed from cartilage and related to the normal resorptive process of bone by osteoclasts which takes place in the histogenesis of these bones. The predominant location of the giant cell tumor in the epiphysis of the long bones, it was seen, was in favor of this view. The fact that the membrane bones of the skull are not involved by either bone cysts or simple giant cell tumors confirms it.

EPULIS

The giant cell epulis of the jaws affords a strenuous proving ground to the concept of giant cell tumor advanced in this paper. For apparently in this group of benign lesions which occur on the gums and about the teeth there is no temporary bone undergoing resorption to stimulate the osteoclastic proliferation. Yet the characteristic giant cell in giant cell tumor is often described by the name of epulis, and under the microscope the basis of such terminology is plainly evidenced by the numerous large giant cells found in these growths.

Varieties.—Under the low power, the presence of stratified epithelium growing downward into the tumor from the mucous membranes of the gum must be relied on to differentiate many of these growths from

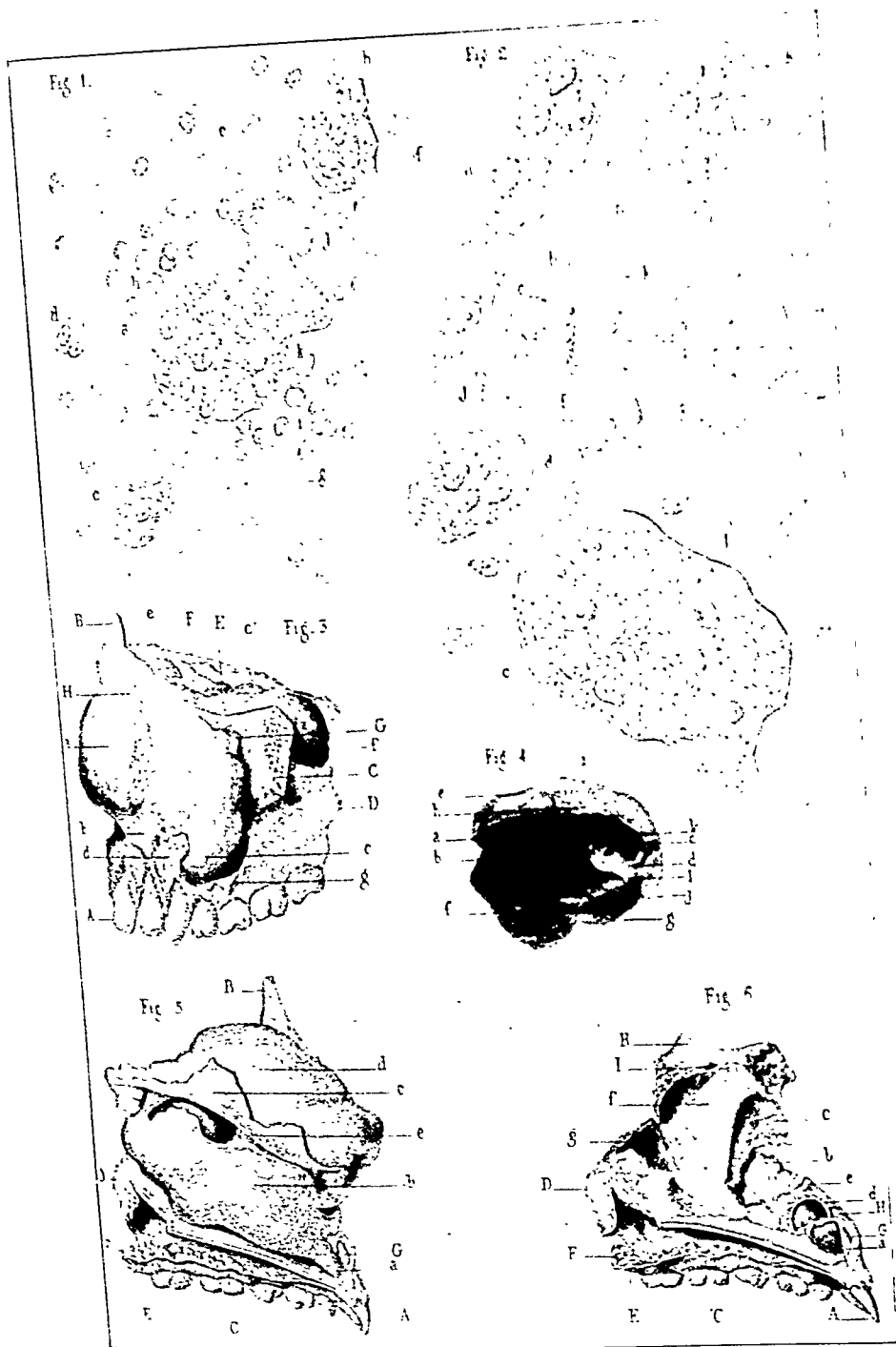


Fig. 46 (from Nélaton: *Tumeurs benignes des os*, 1860).—Illustrations of a tumor arising in the ethmoid bone and presenting through the antrum into the maxilla. The resection of the jaw shows nicely the location of the tumor in the turbinates, which are derived from cartilage. (The capital letters of the alphabet were used by Nélaton to refer to normal structures, the smaller letters to the neoplastic features. Their keys have been omitted because of their irrelevancy here.)

the typical giant cell tumor (fig. 47 *A* and *B*). The giant cells are of the usual multinucleated type and differ from those in the giant cell tumor of the long bones in no important detail. In the stroma of the epulis there is a tendency for a fibrous modification or a leukocytic infiltration to take place, and in special areas new bone formation of the fibro-ostosis type, such as is seen at the margins of the giant cell tumor and in the bone cyst, are frequently seen. These islands of bone are typical osteoid spicules with osteoblasts applied to their surface.

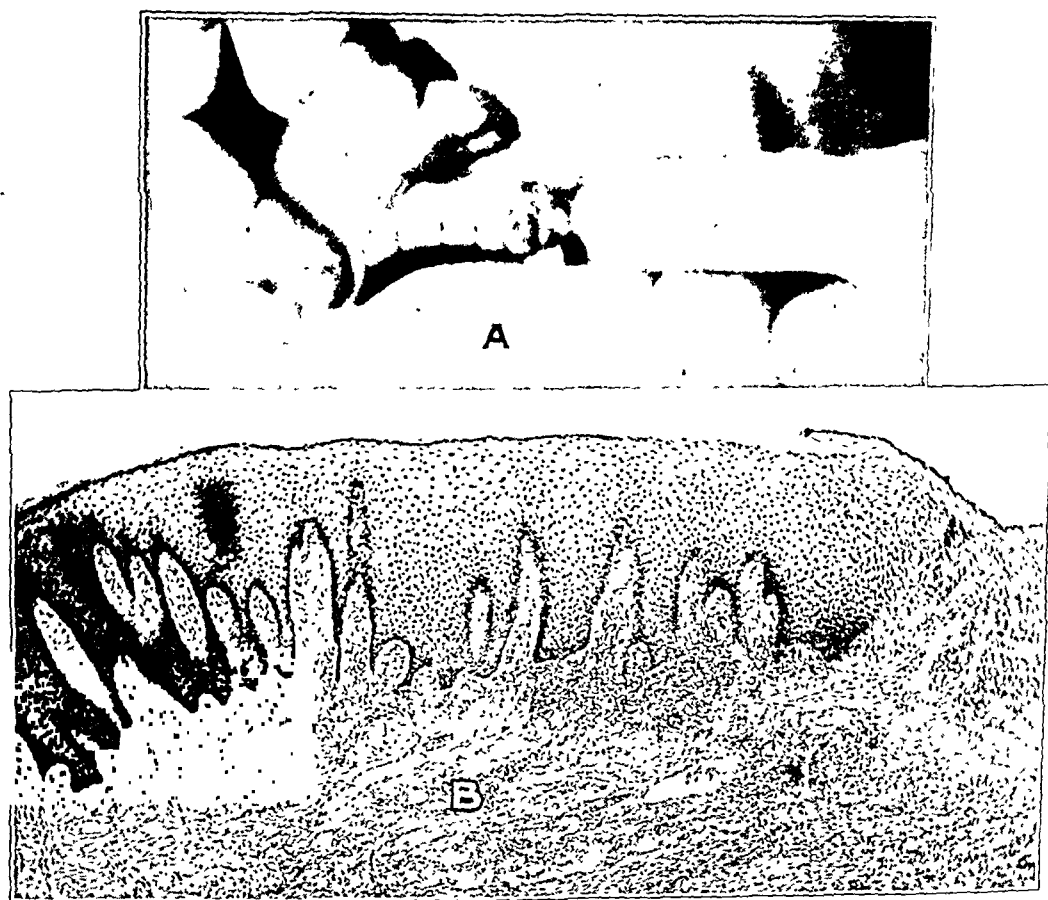


Fig. 47 (nos. 26824 and 36458).—Epulis of the giant cell type on the upper alveolar border. *A* illustrates the gross, and *B*, the microscopic. The giant cell areas are some distance from the mucous membrane and do not show well in this picture.

The foregoing description, however, is varied markedly in the so-called fibroid epulis. Here under the microscope, the tumor is practically always without giant cells. When these occur, they are sparse and small (fig. 48). The stroma is spindle and fibroblastic and in some places it is loose and edematous forming small evacuated cysts. In other places the fibroblasts are being transformed into osteoblasts which are laying down the intercellular substance of osteoid tissue. At points this

osteoid tissue is converted into true bony spicules of the same type seen in osteitis fibrosa. Organized hemorrhage is also present.

Microscopic analysis, therefore, divides epulis into a giant cell variety which is practically indistinguishable in its fundamental histology from giant cell tumor and a fibroid variety, which is the exact homologue of osteitis fibrosa. There are only minute variations such as a slight modification in the morphology of the giant cell in the first class of epulis and the tendency of the second class of epulis to be a solid structure

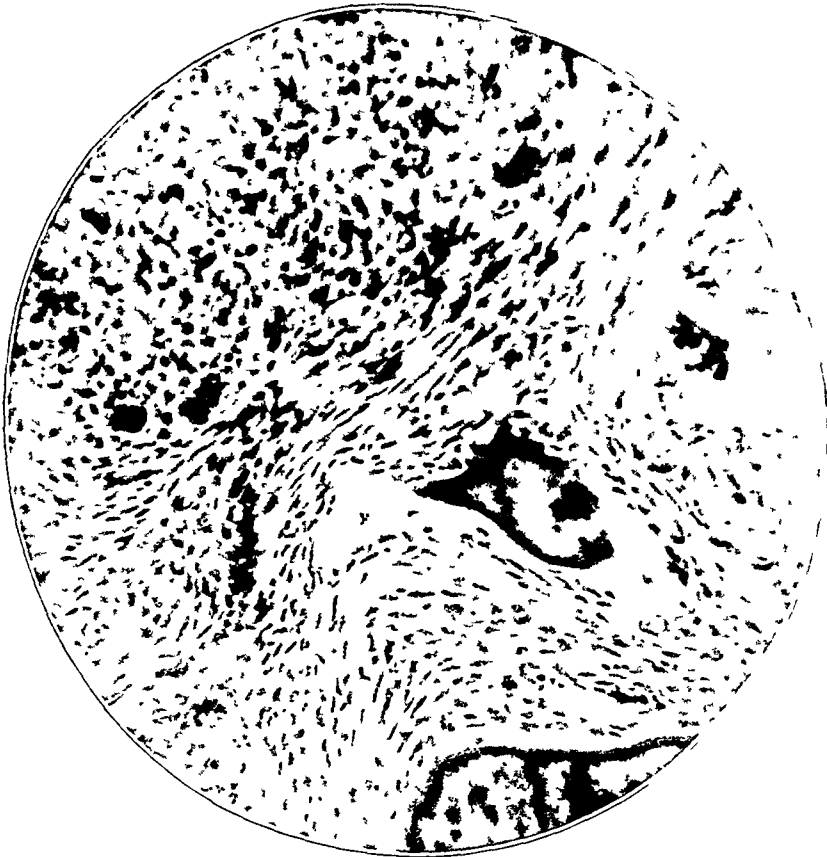


Fig 48 (no. 23768).—Photomicrograph illustrating the fibroid type of epulis. Note the resemblance to osteitis fibrosa.

rather than a thin walled cyst. The conclusion that we are dealing with the same type of pathologic process here as in the cyst and the giant cell tumor in the long bones is unavoidable. Clinically and in the gross, however, the epulis is found only along the alveolar borders of the upper and lower maxillae which are membranous bones, and it is a periosteal rather than a medullary lesion.

These two facts constitute an apparent exception to the rule that giant cell tumor and its healing phase, osteitis fibrosa, always occur in the medulla of intracartilaginous bone as a consequence of a dysfunc-

tion in the normal osteoclastic resorption of this type of bone. The belief that the giant cell tumor is an exaggeration of such osteoclastic activity in the resorption of temporary bone, advanced throughout this paper, contests such an exception to the general rule, and demands that epulis be brought into intimate relationship with a normal osteoclastic hyperplasia.

Origin.—At the outset it is necessary to exclude from a diagnostic standpoint a large number of the cases usually classed as epulis. Many extraneous lesions such as hemangioma, fibroma, fibrohemangioma and fungating ulcers of infectious origin are erroneously placed in this category on the insufficient grounds that they occur on the gums. When this group is restricted on microscopic grounds to the lesions already described under the giant cell and fibroid epulis, a clinical entity is obtained which is more readily analyzed.

Epulides of this restricted category have been shown beyond peradventure to be periosteal in origin. Bloodgood³³ has shown that the lesions arise from the alveolar dental periosteum. They may arise either under the mucous membrane of the gum immediately surrounding a tooth or from the interior of the root socket itself. Besides this close association with the periosteum of the teeth, they occur only at the alveolar borders of the maxilla in the regions extending from the first molar on the one side to the first molar on the opposite side. An epulis practically never occurs behind or fastened to the root of the last molar and rarely at the site of any of the permanent molars. This point was emphasized by Scudder³⁴ in a review of 178 cases compiled from various clinics. They are most frequent near the canine and bicuspid teeth. Clinically, this relation to the teeth is further emphasized by the symptoms of the patient who gives a history of a carious tooth or some other dental irritation. The patient generally refers to the growth in its early stages as a gum boil, but the advanced stages may show a tremendous overgrowth of tissue protruding over the jaw and outside of the oral cavity. The growth of the epulis is outward and practically never invades the bone but pushes upward through the gums in the crevices about the teeth or in a fossa where a tooth has been pulled. The overgrowth and increase in size is never rapid until the tumor has escaped the confines of the alveolar border and is proliferating over the margins of the gum. The patients are most often children or young adults.

It is a consideration of these clinical features of epulis that gives a clue to the pathologic changes in this disease. First, they arise only

33. Bloodgood, J. C., on Epulis, Bryant and Buck: *American Practice of Surgery* 6:818, 1909.

34. Scudder, C. L.: *Tumors of the Jaws*, Philadelphia, W. B. Saunders Company, 1912.

about the periosteal borders of certain teeth. Second, they practically never occur at the site of the molar teeth. Third, they expand outwardly and proliferate only after escaping the alveolar border. Fourth, they occur most frequently in children (not infants) and young adults. Again the age incidence and the site of the lesion are invaluable in disclosing the nature of the pathologic process. The unique features of the age limits and the failure of the epulis to occur about the molars relates these lesions to the deciduous teeth. For unlike all the other teeth the molars make only one appearance and that is a permanent one. If epulis can be related to the normal process of shedding the deciduous teeth which begins at the age of 6 and extends to the thirteenth year, the histogenesis of this process should explain the nature of the epulis and correlate the pathologic changes in this lesion with those in other giant cell tumors. This expectation is fulfilled when a study is made of the embryology of the teeth and the histologic process by which they are shed. Here the hyperplasia of osteoclasts seen in giant cell tumor is duplicated by an analogous process, in which there is a proliferation of odontoclasts that are instrumental in loosening and dissolving the roots of the deciduous teeth.

In more detail the histology is as follows: The anchorage of the deciduous teeth is by means of a thin layer of dental cement or cementum which surrounds the roots and is invested by a periosteal coat (or pericementum) which forms at once the outward coat of the roots and the periosteum of the jaw uniting the one to the other. The pericementum stops at the neck of the tooth and forms an annular thickening in conjunction with the dense connective tissue of the gum that is known as the circular dental ligament. The cementum itself is membranous bone and differs in no essential respect from this type of bone found elsewhere in the body. At about the age of 5 years odontoclasts arising from the pericementum or periosteum of the root proliferate and absorb the cementum of the roots of the deciduous teeth and thus open the way for the eruption of the permanent teeth (fig. 49).

About the roots of the deciduous teeth, therefore, there is a periosteum which is normally endowed with the power of osteoclastic hyperplasia. This osteoclastic hyperplasia is a normal occurrence after the age of 5 and is nature's provision for shedding the deciduous teeth. The process is analogous to the osteoclastic hyperplasia that occurs in the ends of the long bones and in the cartilaginous bones of the skull and is the natural method for the absorption of cartilaginous bone. The deciduous teeth, therefore, are in part like cartilaginous bone in that both are temporary bony structures and the pathologic process of giant cell tumor arises in connection with either, in one case giving origin to epulis and in the other the typical giant cell tumor of the long bones.

The fact that there is a fibroid type of epulis just as there is osteitis fibrosa in relation to giant cell tumor confirms this view. The fibroid epulis is the evidence of the healing reaction of the periosteum about the lesion. This healing reaction, like that everywhere in the periosteum

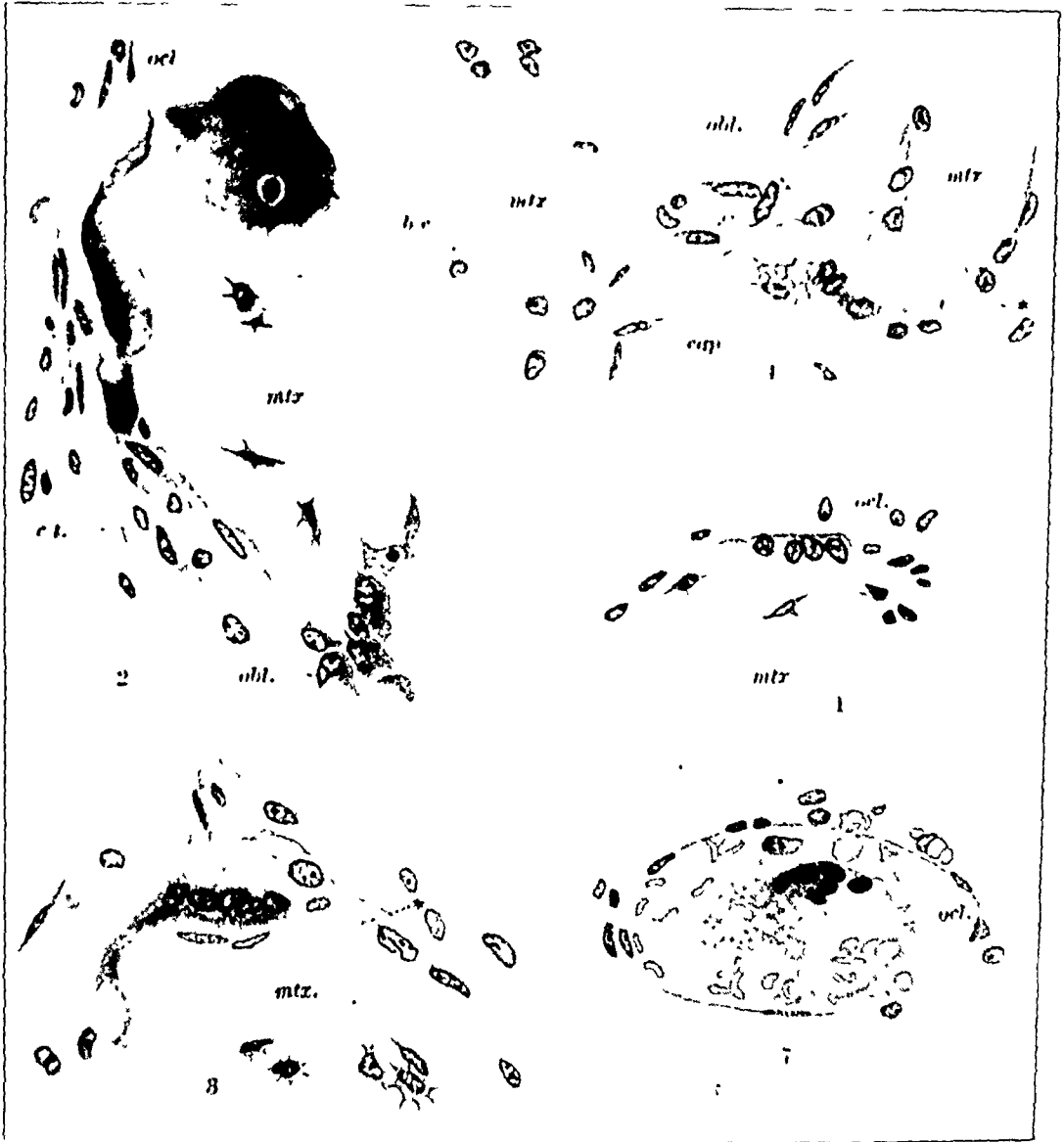


Fig. 49 (after Arey. *Am. J. Anat.* 26:315, 1919-1920).—Giant cell osteoclasts about the roots of the deciduous teeth of young pigs. *ocl.* indicates giant cell osteoclasts; *mtz.*, matrix of teeth roots and *obl.*, osteoblasts.

and subperiosteal layers of bone, is an efficient defense against osteoclastasia or giant cell tumor. We have seen that it is capable of arresting a giant cell tumor or bone cyst in the shaft of a bone. At the epiphysis, however, where periosteum and cortical bone are deficient,

the giant cell tumor is progressive and breaks through. In the same way, in regard to epulis, the fibroid reaction (or as we choose to call it fibro-ostosis) is an efficient barrier to the tumor. It practically never invades the body of the jaw unless there has been undue trauma or some other factor. The ability of the epulis to progress and to proliferate over the gum, however, is due to the fact that periosteum ceases at the surface of the tooth, and it is through this gap about the teeth that the epulis erupts.

There are few other places in the body, to our knowledge, in which the periosteum is endowed normally with such osteoclastic proliferation as it is here at the alveolar border, although it is true as is demonstrated in the absorption of callus after fracture that all periosteum has some osteoclastic power. The unique situation, therefore, of epulis is readily comprehended. These tumors are connected with the shedding of the deciduous teeth, and the age incidence of them is related to the eruption of the permanent teeth as is shown in table 12.

TABLE 12—*Age Incidence of Epulis in Relation to Eruption of Permanent Teeth*

Age of Eruption of Permanent Teeth *		Age Incidence of Epulis †	
First molars	6th year	5 to 10 years	6 cases
Two central incisors	7th year	10 to 20 years	17 cases
Two lateral incisors	8th year	20 to 30 years	7 cases
First premolars	9th year	20 to 45 years	9 cases
Second premolars	10th year		
Canine	11th and 12th year		2 cases
Second molar	12th and 13th year		
Third molar	17th and 25th year		

* Gray's Anatomy, ed 21, 1924, p 1134

† All patients were over 5½ years and under 45 years of age. No lesions occurred at the site of the third molar.

It will be seen that there is a latent period or lag between the appearance of epulis and the shedding of the teeth. In other words there is an elapse of time between cause and effect which is due to the slow and benign course of these lesions. But the important point is that the epulis does not occur before the age of 5, and this is due to the fact that the permanent teeth do not begin to erupt until the age of 6. Instead of being an exception to the rule that giant cell tumor follows on a normal proliferation of osteoclasts, the epulis, therefore, presents valuable evidence in confirmation of this view. These lesions are related to a normal proliferation of the odontoclasts, and the process is best termed odontoclastasia which avoids the confusing miscellaneous group of conditions that for years have been carelessly thrown together under the term of epulis.

XANTHOMA

The view that the giant cell tumor arises as an abnormal phase in the osteoclastic resorption of cartilaginous or temporary bone demonstrates its usefulness when applied to the pathologic changes in the giant cell tumors of the xanthoma group. For here this conception enables

us to disprove the current endothelial and granulation tissue theories of these growths and to split off for the first time a clinical and pathologic entity from this chaotic group of lesions.

Varieties.—Since Lebert,³⁵ in 1845, introduced the term xanthos to denote a group of yellow fibrous tumors, a large and miscellaneous collection of entities has accumulated under that heading. A group of skin lesions under the names of xanthoma palpebrarum, xanthoma diabeticorum and xanthoma multiplex may be set aside here because giant cells are absent and untypical of this series. While containing lipid pigments, blood pigment is usually wanting in these lesions. The xanthomatous tumors connected with the joints and tendons, however, frequently contain typical giant cell areas, and are related to the group of skin lesions mentioned only by their characteristic yellow color which has been shown definitely to be due to blood pigment or lipoids and hence nonspecific. Cells related to these lipoids and containing cholesterol have been referred to in the literature as foam cells and occur just as indiscriminately in this series of tumors as does pigment, being less frequent, but equally nonspecific. These foam cells also accompany at times typical giant cell areas in this collection of growths, and the presence of these cells in otherwise typical giant cell tumors of the long bones has led to the connotation of xanthosarcoma of bone by some authors.

Writers on the subject of xanthomatous tumors are agreed that this group comprises neither a clinical nor a pathologic entity. But since the giant cell areas have been viewed as nonspecific granulation tissue and both pigment and foam cells have been proved to be nonspecific, a criterion has been lacking wherewith to begin the analysis of this group of lesions into separate entities.

Nevertheless, since the time of Chassaignac³⁶ in 1852 and Billroth³⁷ in 1868, clinical peculiarities in regard to giant cell tumors of the tendon sheaths have repeatedly caused them to be set apart in this xanthoma group. More recently Tourneux³⁸ in 1913, Beekman³⁹ in 1915, Broders⁴⁰ in 1917, Garrett⁴¹ in 1924 and Mason and Woolston⁴² in

35. Lebert: *Physiologie et pathologie*, Paris, D. Baillière, 1845, vol. 2, p. 120.

36. Chassaignac: *Gaz. d. hôp.*, 1852, p. 185.

37. Billroth, cited by Beekman: *Giant Cell Tumors of the Tendon Sheaths*, *Ann. Surg.* **62**:739, 1915.

38. Tourneux, J. P.: *Les sarcomes des gaines tendineuses*, *Rev. de chir.* **47**: 817, 1913.

39. Beekman, F.: *Giant Cell Tumors of the Tendon Sheaths*, *Ann. Surg.* **62**: 738, 1915.

40. Broders, A. C.: *Benign Xanthic Extraperiosteal Tumor of the Extremities Containing Foreign Body Giant Cells*, *Ann. Surg.* **70**:574, 1919.

41. Garrett, C. A.: *Tumors of the Xanthoma Type*, *Arch. Surg.* **8**:882 (May) 1924.

42. Mason, M. L., and Woolston, W. H.: *Isolated Giant Cell Xanthomatic Tumors of the Fingers*, *Arch. Surg.* **15**:499 (Oct.) 1927.

1927 have emphasized the tendency for these tumors to occur on the hand about the fingers and on the foot and about the ankle. Although the exact limits of the group were pathologically ill defined, Mason and Woolston ⁴² were able to collect 144 cases including eight of their own, placed in this class with reasonable assurance on the grounds of their characteristic location and peculiar histology. The clinical summary by these authors shows that the sexes are about evenly affected, that adults with an average age between 35 and 40 predominate, and that the size of these firm yellow tumors ranges between that of a pea and that of an egg. The course of the disease is typically benign but protracted

TABLE 13.—*Giant Cell Tumors of Tendon Sheaths*

Path. No.	Race, Sex, Age	Location	Trauma	Duration	Microscopic
4265	W. M. 38	Little finger, flexor surface.....	6 years	Typical giant cell areas
4193	W. F. 59	Index finger	Typical giant cell areas
4103	W. M.	Finger	Typical giant cell areas
4659	W. F.	Ring finger, flexor surface.....	4 years	Typical giant cell areas
3678	W. F. 16	Thumb, ulnar side.....	Typical giant cell areas
3623	W. F. 13	Ring finger, flexor surface.....	Yes	13 months	Typical giant cell areas
3599	W. M. 38	Index finger, extensor surface....	Yes	5 years	Typical giant cell areas
3523	W. M. 17	Middle finger	Typical giant cell areas
3451	W. M.	Index finger, flexor surface.....	2 years	Typical giant cell areas
3260	Finger	Typical giant cell areas
3240	W. M. 35	Index finger, flexor surface.....	Yes	1 year	Typical giant cell areas
3155	W. M. 7	Great toe, medial side.....	4 months	Bone and giant cell areas
2645	W. F. 39	Index finger, flexor surface.....	3 years	Typical giant cell areas
2597	W. F. 27	Middle finger, flexor surface....	10 weeks	Typical giant cell areas
2559	W. M. 59	Index finger, flexor surface, ring finger	1 year	Typical giant cell areas
2710	W. F. 18	Ankle	Typical giant cell areas
2612	W. F. 73	Middle finger, multiple.....	Yes	3 years	Typical giant cell areas
21328	W. M. 24	Ring finger, flexor surface.....	Yes	5 years	Typical giant cell areas
5814	W. M. 45	Foot, metatarsal	30 years	Cartilage and giant cell areas
1929	W. M.	Hand	Typical giant cell areas
1773	W. F. 58	Foot, instep, tarsal bones eroded	14 years	Typical giant cell areas
1727	W. M. 50	Ankle	Yes	3 years	Typical giant cell areas
14718	W. F.	Finger	Typical giant cell areas
1164	W. F. 56	Index finger	Typical giant cell areas
9137	W. M. 23	Foot	Typical giant cell areas
2399	W. M. 30	Thumb, flexor surface.....	Yes	18 years	Typical giant cell areas
1629	W. M. 46	Ankle, medial side.....	22 years	Typical giant cell areas

(average duration four and one-fourth years), while trauma as an etiologic factor is present in from 30 to 60 per cent of the cases.

We have restudied this group of tumors and have had the privilege of checking the studies made by Garrett ⁴¹ in this laboratory in 1923 who reviewed 196 lesions of the joints, bursae, tendons and of the subcutaneous tissues. Our restudies with over 100 additional cases in the same groups accumulated since that time permit a segregation of twenty-seven lesions with a xanthic color composed of fairly typical giant cell areas, and the group thus histologically restricted presents more forcibly certain clinical and pathologic peculiarities.

As shown in table 13, eighteen of the twenty-seven lesions were located on the fingers at the metacarpophalangeal or interphalangeal

joints, and most of these were on the flexor surface. The remainder with few exceptions were elsewhere on the hand or about the foot and ankle. This predilection of the tumors for the tendons in special regions only is of more than passing significance.

Not only are the localities involved unique, but the histologic structure of these lesions is equally striking. Fibrosis of a marked degree akin to the spindle cell variant of giant cell tumor or to the fibroid type of epulis predominates the stroma about the giant cell areas. This

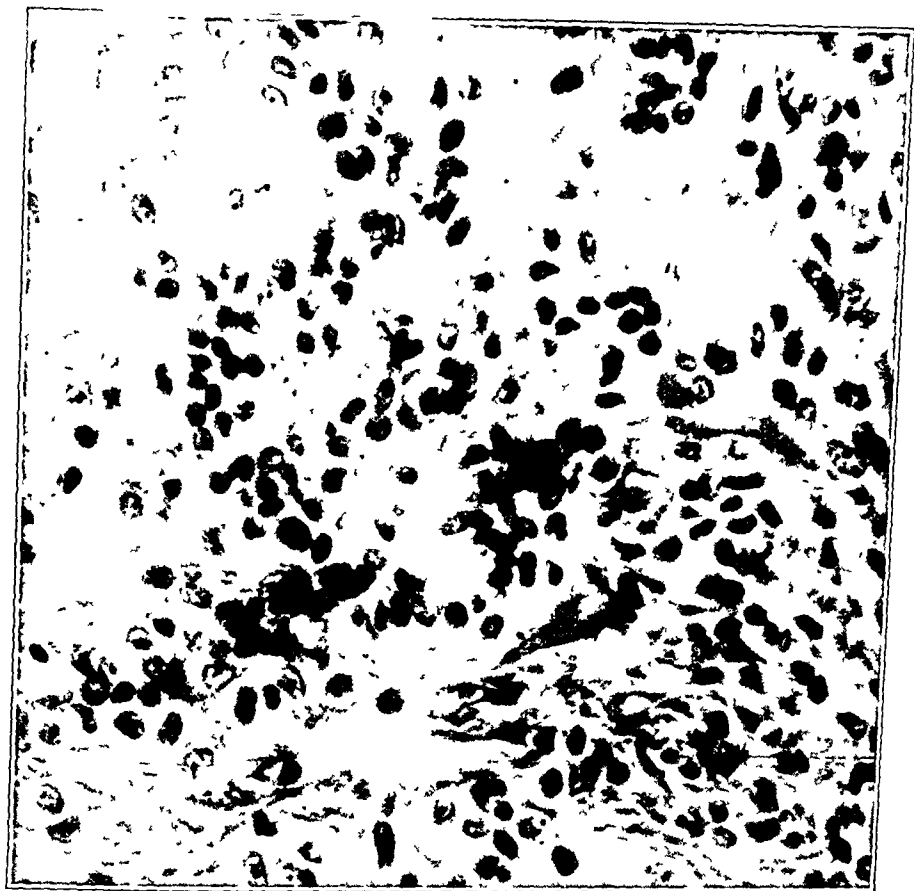


Fig 50 (no. 42995) —Photomicrograph showing the high power of a giant cell xanthoma of the tendon sheaths. Note the network of intercellular substance, the giant cells and the numerous round cells. A few larger cells resembling cartilage cells are seen among the fibrous network.

fibrous tissue takes an unusually brilliant pink stain with hematoxylin and eosin and forms a peculiar lattice work in special areas enclosing cells that resemble cartilage cells (fig. 50). Giant cells of the usual epulis type, large and multinucleated, are numerous, and frequently average more than 30 to a low powered field. They are embedded in the usual round cell stroma typical of giant cell tumor, and conspicuously not the round cell infiltration seen in granulation tissue. Occasionally,

the foam cell characteristic of other types of xanthoma is present, but this type of cell has also been observed in 5 per cent of the giant cell tumors occurring in the long bones.

Under the microscope, pigment is a conspicuous feature of most of these tumors. As Smith⁴³ showed by his studies in this laboratory, this pigment is old blood pigment and gives the typical iron reaction.

Since we reject on histologic grounds the current granulation tissue theory of these lesions, it is necessary for us to demonstrate a connection between these tumors and some bony or cartilaginous structure. Heretofore attempts to establish such a relationship have failed, since tendons attach to the fibrous layer of the periosteum and bone only at their distal ends and the tumors under discussion are found not at this point, but in a more proximal position within the tendon sheaths.

Origin of Xanthoma of the Tendon Sheaths.—Fortunately there was available in the laboratory an important clue. A giant cell tumor of the patella was on record (table 7). Seven such tumors of the patella recorded as variants of either the bone cyst or the giant cell tumor have been reviewed by Cole,⁴⁴ and a personal communication from King and Towne⁴⁵ described a similar tumor of the patella the report of which has been published in the ARCHIVES OF SURGERY. The microscopic appearance of these tumors of the patella resembles the giant cell tumor of the tendon sheaths in regard to the large amount of pink-staining fibroid material. Still more important is the fact that the location of these tumors resembles the site of origin of similar tumors in the xanthoma group, in that the patella is embedded in a tendon, being a true sesamoid bone derived from cartilage.

The immediate inference suggested is that the giant cell tumors of the tendon sheaths arise in the sesamoid bones. The fact that these bones are derived from cartilage brings this inference into line with the conception of giant cell tumor pointed out in this paper and the fact that these sesamoid bones occur more frequently in the tendons of the fingers coincides with the location of these tumors described clinically.

A review of the embryology and anatomy of the sesamoid bone occurring in the human body supports the view that the giant cell tumor of the tendon sheaths arise from these bones. These bones must be regarded according to Thilenius⁴⁶ as integral parts of the skeleton

43. Smith, D. T.: Method for Making a Differential Diagnosis Between Xanthomatous and Melanin Tumors from Frozen Sections, Arch. Surg. 8:908 (May) 1924.

44. Cole, W. H.: Primary Tumors of the Patella, J. Bone & Joint Surg. 7: 637, 1925.

45. King, M. J., and Towne, G. S.: Primary Giant Cell Tumor of the Patella, 18:892 (March) 1929.

46. Thilenius, cited by Bradley, O. C.: Anat. Anz. 28:528, 1906.

phylogenetically inherited. Bradley⁴⁷ has shown that embryologically these bones are cartilaginous buds separating off from the joint side of the future bone just beneath the flexor tendon (fig. 51). The work of Pftzner⁴⁸ has shown that the sesamoid bones are most frequent on the first, second and fifth digits of the hand and foot at the metacarpophalangeal or the metatarsophalangeal joints, but that they may occur at the site of these joints or the interphalangeal joints in all of the fingers and toes. Other, but more unusual, sites are in the tendons about the elbows, knee or ankle and in the tendon of the psoas muscle at the pubis

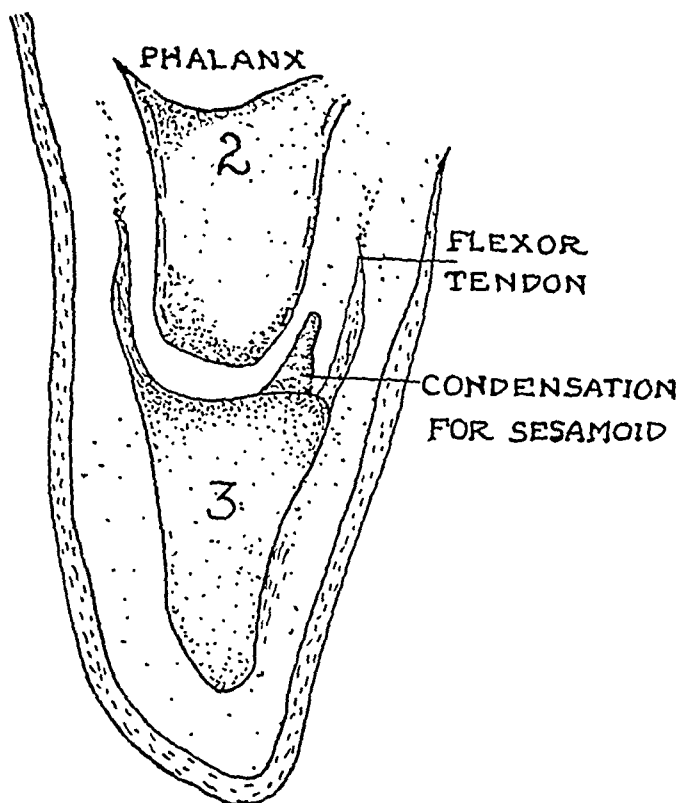


Fig. 51 (after Bradley: *Anat. Anz.* **28**:528, 1906).—Sketch showing the development of a sesamoid bone on the flexor side of a digit in a pig embryo 52 mm. long of forty days' gestation. The sesamoid bone, preformed in cartilage, is seen budding from the joint side of the distal phalanx.

or occasionally in the gluteus maximus near the head of the greater trochanter (table 14 and fig. 52).

In a study of the twenty-seven cases of giant cell tumors of the tendon sheaths in our own series and in a review of cases reported in

47. Bradley, O. C.: A Contribution to the Development of the Interphalangeal Sesamoid Bone, *Anat. Anz.* **28**:528, 1906.

48. Pftzner, W.: Die Sesambeine des Menschen, *Morphol. Arb.* **1**:517, 1892.

the literature, all of those cases having typical giant cell areas were found to coincide in location with the sites of sesamoid bones. The occurrence of the sesamoid bones most frequently on the flexor surfaces of the fingers of the right hand is duplicated by these tumors. Mason and Woolston⁴² in their review of 144 cases found the flexor surfaces of the fingers of the right hand most frequently affected, sixty-four of seventy-four tumors occurring on the flexor surfaces. On the lower extremities there is a similar coincidence in location, the xanthic giant cell tumors here occurring about the malleoli at the ankle and along the toes at the site of sesamoid bones. In the cases reported in the literature in which these xanthic tendon sheath tumors do not occupy the site of sesamoid bones, the microscopic reports show that they do not have the typical giant cell structures⁴⁹ and that they belong more properly to the fibrohemangiomas, fibromas or ganglion class, a point of

TABLE 14.—*Location of Sesamoid Bones in Man*

In the Upper Extremity	In the Lower Extremity
Flexor surface of the hand	Plantar aspect of the foot
Metacarpophalangeal joint—thumb	Metatarsophalangeal joint—great toe
Metacarpophalangeal joint—index finger	Metatarsophalangeal joint—second toe
Metacarpophalangeal joint—little finger	Metatarsophalangeal joint—little toe
Metacarpophalangeal joint—middle finger	Metatarsophalangeal joint—third toe
Metacarpophalangeal joint—ring finger	Metatarsophalangeal joint—fourth toe
Interphalangeal joint—thumb	Interphalangeal joint—great toe
Interphalangeal joint—Index finger	Interphalangeal joint—rarely second toe
Other Locations	
Arm: Biceps brachii at radial tuberosity	
Leg: Patella in quadriceps, peroneus longus at cuboid; tibialis anticus at first cuneiform; tibialis posticus at talus; head of gastrocnemius at lateral condyle of femur; psoas at pubis; gluteus maximus at greater trochanter; ankle tendons at both malleoli	

view confirmed by our studies of more than 300 cases of this variety in the surgical pathologic laboratory.

The most convincing evidence that the sesamoid bones are the source of origin for these growths, however, is presented by the histology of the tumors themselves, for some vestige of the original structure of the sesamoid bones is usually visible under the microscope.

Special study on this point reveals the fact that the pink-staining network of tissue observed in the sections is the remains of white fibrocartilage from which tissue the sesamoid bones are known to be derived. The presence of this stroma containing cartilage cells confirms the origin of these tumors from the sesamoid bones. In several cases the calcification of this cartilage and transformation to bone were observed in the sections (fig. 53).

49. Since this paper was written the article by R. S. Rowland on "Xanthomatosis" has appeared (Arch. Int. Med. 42:611 [Nov.] 1928). The erosion of the skull bones described by him is due to the tumors in the dura, and the few giant cells observed are phagocytizing dead bone, and are secondary to, rather than primary in, the xanthomatous tumors of the dura. Sections sent to the authors through the courtesy of Dr. Rowland do not show giant cell tumor.

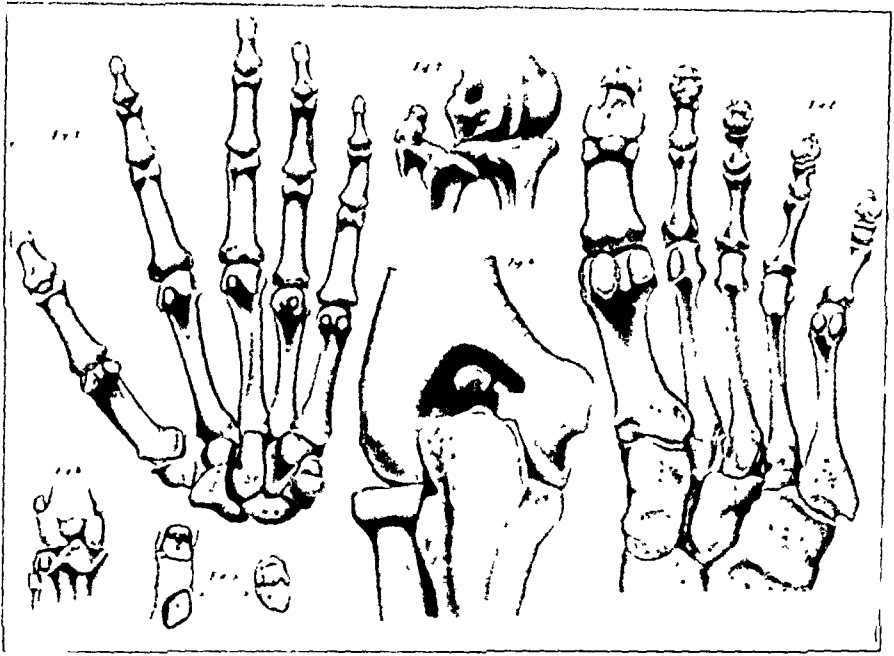


Fig. 52 (after Plützner: *Morphol. Arb.* 1:517, 1892).—Anatomic preparations showing sesamoid bones in most of the localities in which they occur on the hand and foot and at the knee and elbow. Sesamoid bones occurring about the ankle are not shown in this illustration.



Fig. 53 (no. 31888).—Tumor of the sesamoid bone on the great toe. Bone derived from cartilage surrounded by giant cells is shown in the high powered photomicrograph. This tumor of the xanthoma group became infected and showed a healing reaction similar to osteitis fibrosa.

The peculiar yellow color of these tumors that has attracted so much attention differs from the deeper russet color of the giant cell tumor of the long bones because of changes in the blood pigment associated with age. These xanthic tumors have a much longer duration of symptoms (fifty months average duration as compared with fourteen months for giant cell tumors of the long bones), and their limited size is due to the small size of the bones affected and the resistance of the fibrous encapsulation, derived from the tendon sheaths. Adjacent bones are eroded on the side opposite the tendon sheaths, however, as is frequently recorded in the operative notes from many different clinics. In these small bones, compact bone, which promotes ultimate healing, is wanting, and a slow protracted course is the result.

From the foregoing it is seen that giant cell tumors of the tendon sheaths, which have long been erroneously classed under the heading of xanthoma are in reality tumors of the sesamoid bones, rather than of soft part structures. These sesamoid bones which are derived from fibrocartilage when affected by giant cell tumor emphasize again the relation of osteoclastic proliferation in bone newly formed from cartilage to the giant cell tumor.

The Xanthoma Variant of the Giant Cell Tumor of Bone.—Xanthoma or foam cells appear occasionally in giant cell tumors of the long bones. In the series of giant cell tumors (exclusive of those of the tendon sheaths) reviewed in this paper, these characteristic foam cells were found in only nine cases (fig. 54 A). These cells never predominated the picture and were relatively scarce, the tumor in the gross resembling the ordinary giant cell tumor. Although a case of xanthosarcoma of bone as described by Ewing⁵⁰ has never been observed in our series, we have noted foam cells in two cases of osteogenic sarcoma (fig. 54 B). Both of these cases have been reported in the literature, one by Goforth⁵⁰ and the other by Stone and Ewing,⁵¹ with the diagnosis of malignancy in giant cell tumor. No note was made on the presence of the foam cells by these authors, but we observed them in a restudy of the sections.

A review of the nine cases of giant cell tumor with foam cells brings out nothing of significance other than the fact that the bone shell is perforated in these instances. The histology resembles that of the typical giant cell tumor without xanthoma cells, and clinically there are no unique features. The presence of two recurrent giant cell tumors and two so-called metastatic giant cell tumors in this series of xanthoma

⁵⁰ Goforth, J. L.: Giant Cell Tumor of Bone. Arch. Surg. 13:846 (Dec.) 1926.

⁵¹ Stone, W. S., and Ewing, J.: An Unusual Alteration in the Natural History of a Giant Cell Tumor of Bone. Arch. Surg. 7:280 (Sept.) 1923.

variants is to be associated with the perforation of the bone shell by such lesions and not with an increased malignancy. The xanthoma cells are the results of the inclusion of lipoids from the soft parts about the tendons where the tumor is infiltrating, and obviously it is the extent of the destruction of the bony shell of the tumor and not the chance presence of foam cells that has clinical significance.^{51a}

Giant Cell Tumors of the Soft Parts.—Because of their relation to the sesamoid bones a brief note is included here on so-called giant cell tumors of the soft parts. The records of only three such cases are available to us at this time. Two of these cases are from the surgical pathologic laboratory, and one is from the literature. In all of these cases we were able by location to relate the tumors to preceding bone.

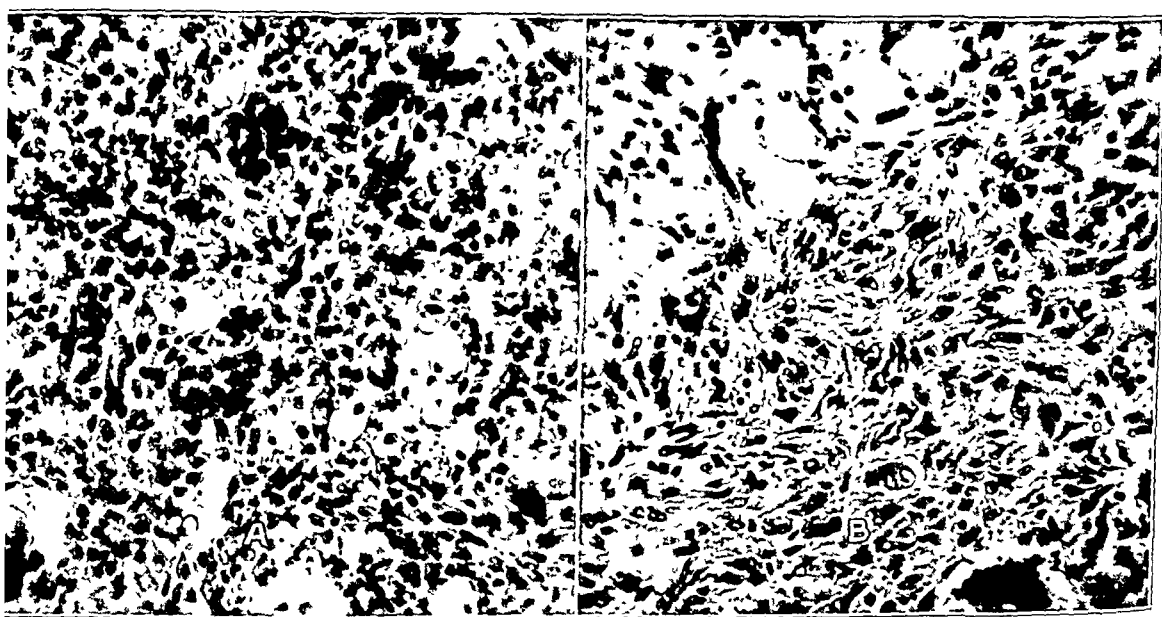


Fig. 54 (nos. 38238 and 40766).—Photomicrographs showing *A*, xanthoma cells in a typical giant cell tumor in the lower end of the radius, and *B*, xanthoma cells in an osteogenic sarcoma in the upper end of the tibia. The bony shell about the tumor was perforated in both cases.

The condition in the first case was diagnosed clinically as a recurrent mixed tumor of the parotid gland (fig. 55). The patient was a white woman, aged 23, with a tumor near the left ear of three years' duration. An incomplete removal of the growth had been performed eighteen months previously, and at the second operation a tumor the size of a

51a. The connection between the foam cells in these tumors and the lipoids derived from the tendons has been confirmed by a study recently called to our attention and published by Kusnetzowski (Virchows Arch. f. path. Anat. 263:205, 1927).

hen's egg was found wedged in between the mastoid process and the angle of the jaw about the stylomandibular ligament. The pathologic diagnosis at that time was xanthoma of the parotid gland. A restudy of this case in this laboratory four years afterward showed it to be a giant cell tumor of the styloid process arising from the lower portion of the bone which has a separate center of cartilaginous ossification, and to which the stylomandibular ligament is attached. Thus the giant cell

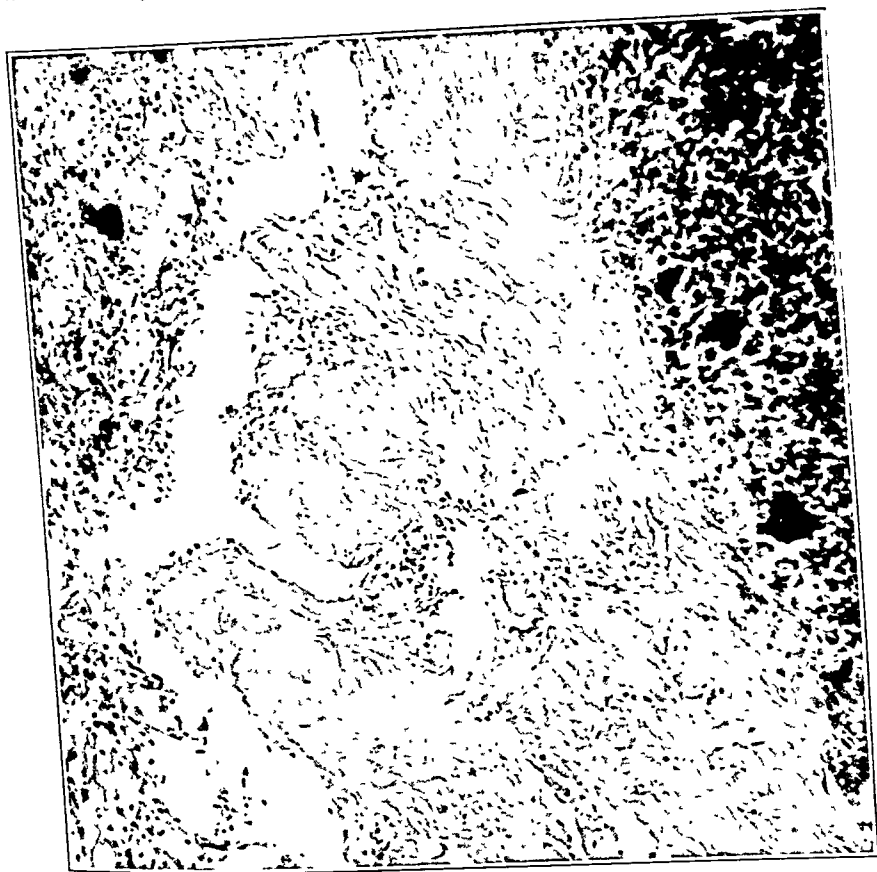


Fig. 55 (no. 35631).—Photomicrograph of a so-called xanthomatous tumor of the parotid gland. This tumor proved to be a giant cell tumor with foam cells arising from the styloid process of the temporal bone.

tumor tissue was related to cartilaginous bone and the foam cells in the tumor associated with a ligamentous structure.

The other two cases are related by location to sesamoid bones. One of these was described by Mallory,²⁸ who observed, "Foreign body giant cells are sometimes produced in such large numbers in reparative lesions not connected with bone that they may suggest a so-called giant cell sarcoma. An illustration of such an appearance is given for comparison. The giant cells followed some destructive lesion of the fat tissue over

the pubes (plate 28, figure 4)." This most extraordinary location coincides with the site of a sesamoid bone in the tendon of the psoas muscle where it glides over the pubic bone. Unfortunately, the unusual site of the lesion did not excite the curiosity of the author.

The last case is similar to this one of Mallory's in that it occurred in the head of the gastrocnemius muscle at the site of a sesamoid bone. Under the microscope the remains of the sesamoid bone were clearly visible, although the tumor had been diagnosed five years previously as a probable sarcoma of the soft parts.

While we have observed giant cells about bone displacing calcified necrotic tissue in tumors of the soft parts, as in the breast, we have never found typical giant cell tumor in such a locality, and we doubt that this tumor ever occurs under such conditions.

SUBPERIOSTEAL GIANT CELL TUMORS

Beside the giant cell tumors of the skull, of the alveolar borders and those of the sesamoid bones, another group of lesions assume a location significant for the interpretation of the pathologic nature of giant cell tumor. This group is the subperiosteal giant cell tumor which occurs in the shaft of the long bones and which presents certain unusual features that bear directly on the etiology of the lesions that we have been considering.

The subperiosteal giant cell tumor comprises a group of extremely modern recognition. Although periosteal giant cell tumors are described in older case reports, such cases on careful analysis prove to be typical giant cell tumors that have perforated their bony shell and grown extra-cortically with a fibrous reaction overlying them. The major portion of such tumors lies within the bone. What is here described as a subperiosteal giant cell tumor is a lesion beneath the periosteum that does not invade the bone to any significant extent. Only four such cases are in this collection, and lesions described of a similar nature are rarely reported in the literature. There is one excellent report by Cone⁵² who described it as an ossifying hematoma. In this contribution the author who has long devoted himself exclusively to the study of pathologic changes in bone had the perspicacity to observe that "osteitis fibrosa, hemorrhagic osteomyelitis and giant cell tumor of bone have their representations in the microscopic pathology of this ossifying hematoma."

The data for the four cases comprising this series are summarized in table 15. In addition to the unique location of the lesions beneath the periosteum of the shaft the striking features brought out are: (1) the short duration of the symptoms (from two to eight weeks); (2) that trauma was the usual initial symptom and (3) that all cases have been recorded since January, 1926.

52. Cone, S.: Ossifying Hematoma, *J. Bone & Joint Surg.* **10**:474, 1928.

Evidently the diagnosis of subperiosteal giant cell tumor is dependent on an early roentgen examination of the patient following trauma. In the roentgenogram the periosteum is raised by a tumor casting little or no shadow which resembles a subperiosteal hematoma (fig. 56). At the operation an extremely thin capsule or shell of bone described by most operators as a blue dome presents itself, and when incised a cystic cavity containing blood is found. Tissue removed from this cavity and examined under the microscope shows a structure of typical giant cell areas intermingled with osteitis fibrosa. In every case there was uncertainty whether the condition should be termed a cyst or a giant cell tumor (fig. 57).

The explanation of these lesions is illuminating, their short duration, their clear relation to trauma and their appearance under the microscope yielding valuable information in regard to the sequence of the pathologic

TABLE 15.—*Subperiosteal Osteoclastasia* *

Path. No.	Race, Sex, Age	Site	Duration	Treatment	Microscopic
3742	W. M. 17	Femur cortical.....	6 weeks	Curetted	Giant cell areas, osteitis fibrosa
3372	W. F. 21	Ulna subperiosteal.....	8 weeks	Excision	Giant cell areas, osteitis fibrosa
3226	W. F. 58	Humerus subperiosteal.....	2 weeks	Curetted	Giant cell areas, osteitis fibrosa
40124	W. F. 16	Humerus cortical.....	8 weeks	Excision	Giant cell areas, osteitis fibrosa

* All lesions were observed since January, 1926.

events. In these cases it is clear that trauma and hemorrhage followed by separation of the periosteum (with a subperiosteal osteogenic layer of tissue) are the initial pathologic events. In the cortex beneath, a disturbance in the periosteal blood supply must occur, and in the periosteum above, some sort of healing reaction is sooner or later stimulated. The result is the mixture of giant cell areas and osteitis fibrosa which are seen under the microscope. That both factors are concerned in healing in this region is exemplified by callus formation and its resorption which forms commonly after most fractures. It is well known that an exuberant callus laid down by the periosteum will be eventually resorbed by osteoclastic activity. In the group of lesions under discussion the osteoclastasia that arises as a result of injury is rapidly regressive. The healing power of the underlying cortical bone and the overlying periosteum is evidently sufficient to heal over any abnormal activity of the osteoclasts. For this reason the duration of symptoms is short, and unless the patient comes under observation soon after injury and a roentgen examination is made, the lesions regress unrecognized, and disappear entirely or in unusual cases persist as a healed exostosis.

Our interest in these lesions is in the relation of hemorrhage following trauma to osteoclastasia. Evidently hemorrhage and a disturbance of the normal blood supply of bone act as a stimulus to the proliferation of osteoclasts and may in some cases lead to an abnormal osteoclastasia, or giant cell tumor. This conclusion means that in the study of the blood supply of the region of the epiphysis and in the factors that may disturb its normal functioning is to be found an explanation of the origin of the giant cell tumor. Some imbalance must arise in the rela-

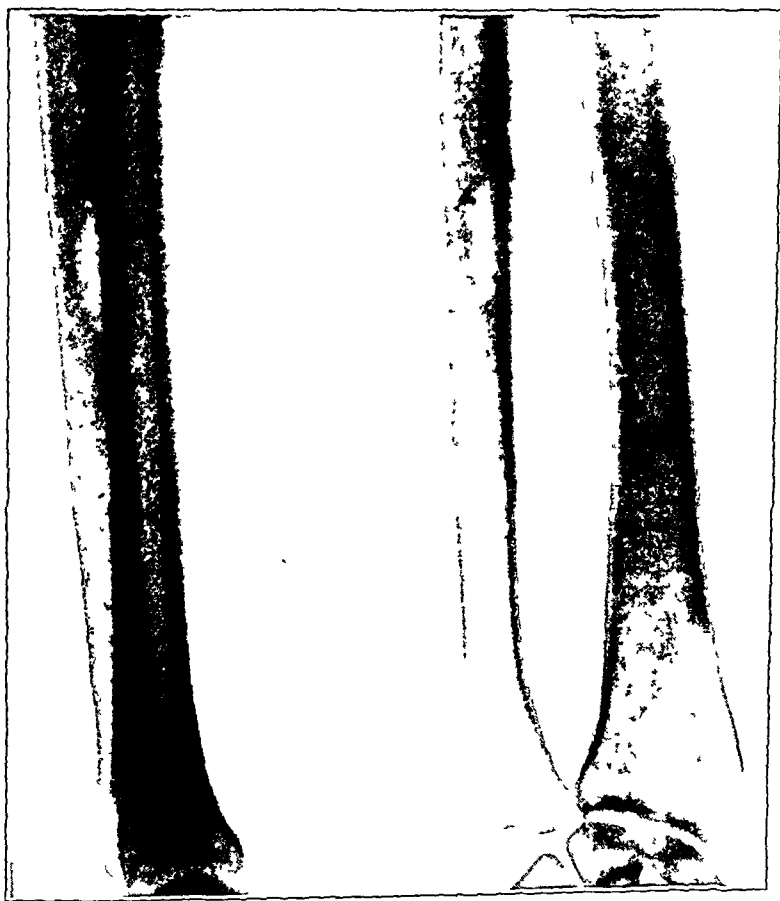


Fig. 56 (no. 38372).—Anterior and lateral x-ray views of subperiosteal osteoclastasia occurring in the shaft of the ulna. The lesion is eight weeks old.

tionship between the proliferation of osteoclasts and the reaction of fibro-ostosis, for apparently it is these two processes that participate in the healing of bone after injury and hemorrhage.

ETIOLOGY OF GIANT CELL TUMOR

It is much easier to discuss the etiology of tumor in terms of so-called etiologic factors than it is to point out the initial event and a subsequent unbroken chain of histologic consequences. For this reason,

the literature abounds with references to the etiologic factors of trauma and hemorrhage in the production of giant cell tumor and bone cysts. Konjetzny,²⁰ Lubarsch⁵³ and Pommer⁵⁴ are among those of the German school that have attempted to trace the bone cysts to medullary hemorrhage following trauma. We are in accord with these authors in placing



Fig. 57 (no. 39293).—Subperiosteal osteoclastasia of two weeks' duration. The photomicrograph shows the giant cells in relation to a newly formed blood cavity. Young fibrous tissue is attempting to repair the lesion. Microscopically, the tissue represents a borderline between giant cell tumor and osteitis fibrosa.

53. Lubarsch: Die Bedeutung des Traumas zur Entstehung und Wachstum krankhafter Gewächse, *Med. Klin.* **41**:1651, 1912.

54. Pommer, G.: Zur Kenntnis der progressiven Hæmatom und Phlegmasieveränderungen (H. v. Haberers), *Arch. f. Orthop. u. Unfall. chir.*, 1920, vol. 17.

trauma in a primary position in the production of these lesions. An attempt will be made, however, on the grounds of the embryologic observations pointed out earlier, to show just how trauma acts histologically in producing the bone cyst and the giant cell tumor.

Relation of Osteoclastasia to the Interruption of the Periosteal Blood Supply.—In the embryo, permanent compact bone is laid down by the perichondrium or subperiosteally, and, as we have seen, this cortical bone is a stronghold for the healing reaction of fibro-ostosis after injury. For nourishment, this bone is partially dependent on the periosteal blood supply. In young adults, this subperiosteal region is an extremely vascular and active tissue, and new bone formation proceeds here more rapidly than elsewhere. On the other hand, the most primitive cancellous bone in the medulla which undergoes reconstruction even in young adults by osteoclastic activity to form the medullary cavity is nourished by vessels in the medulla, the origin of which is from the nutrient artery. This cancellous bone of the epiphysis is supplied from vessels which anastomose around the joint, the diaphyseal, the metaphyseal and the epiphyseal, but as pointed out by Poland²¹ and shown in injected specimens (fig. 58) by Lexer,⁵⁵ these vessels concerned with the major portion of the nutrition of both epiphysis and metaphysis pursue a periosteal and transcortical route.

The significance of this vascular arrangement in the origin of osteoclastasia has been implied in the discussion of subperiosteal giant cell tumor following trauma. The evidence in that group of lesions points to the fact that a vascular disturbance following trauma is a primary factor in the etiology of giant cell tumor.

A unique observation in regard to the site of early lesions of progressive osteoclastasia must now be recalled. Early giant cell tumors in the epiphysis (with a short history of trauma from two to six months previously) practically always assume an asymmetrical and subcortical location. In other words the giant cell tumor, and also the early bone cyst arise at a point just beneath the traumatized area of the cortex. This was pointed out in the study of the x-ray pictures and the gross specimens of these lesions and is again illustrated in the case shown in figure 59. Here the lesion is near the surface of the bone in one of the condyles of the femur. There was a definite history of trauma only two months previously as compared to the average duration of symptoms of fourteen months in giant cell tumor. The import of this subcortical location of the initial epiphyseal lesion has apparently been overlooked heretofore because the giant cell tumor during a later stage enlarges centrally at the expense of cancellous bone rather than out-

55. Lexer, E.: Die Entstehung entzündlicher Knochenherde, Arch. f. klin. Chir. **71**:1, 1903.

wardly against the more resistant cortical bone. The realization that the classic early giant cell tumor of from two to six months' duration practically always gives a history of trauma and shows a lesion sub-cortically at one side of the epiphysis furnishes an important clue to the etiology of this tumor. The site of the early lesion in relation to trauma suggests the cause of the imbalance in bone formation and bone destruction already referred to and demonstrates the sequence of events leading to progressive osteoclastasia.

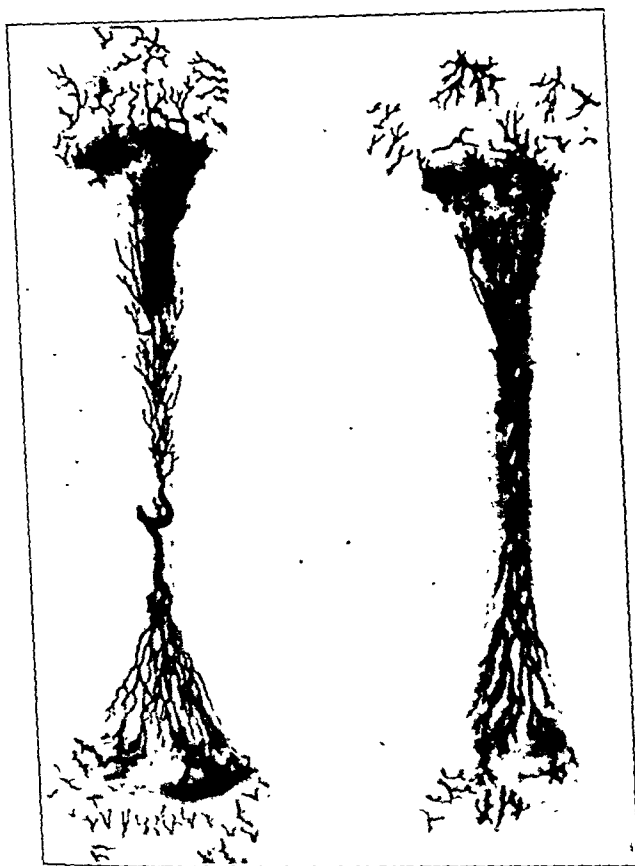


Fig. 58 (after Lexer: *Arch. f. klin. Chir.* 71:1, 1903).—Injected specimens showing the epiphyseal blood supply in the long bones. The femur and tibia are represented.

Because of the prominence of the club-shaped epiphyseal region the cortical or outward edge receives the brunt of the trauma in this locality. This trauma acts mainly on the cortex in relation to its periosteum, avulsing the latter and interrupting the blood supply of the cortical bone. Normal vascular channels are thus supplanted by a subperiosteal hematoma. The effect of this interruption of the periosteal blood supply is to render inactive the cortical bone on this side of the epiphyseal end,

and the normal healing powers of this portion of the bone are suspended. The medullary circulation in the region of the epiphysis must take up an increased activity and by establishing new channels it works its way around the injured area to undertake the work of repair.

This increased function of the medullary blood supply during the interruption of the periosteal circulation can take place only after osteoclasts have opened up the channels in bone for the budding capillaries (for this we have seen is the normal order in histogenesis).

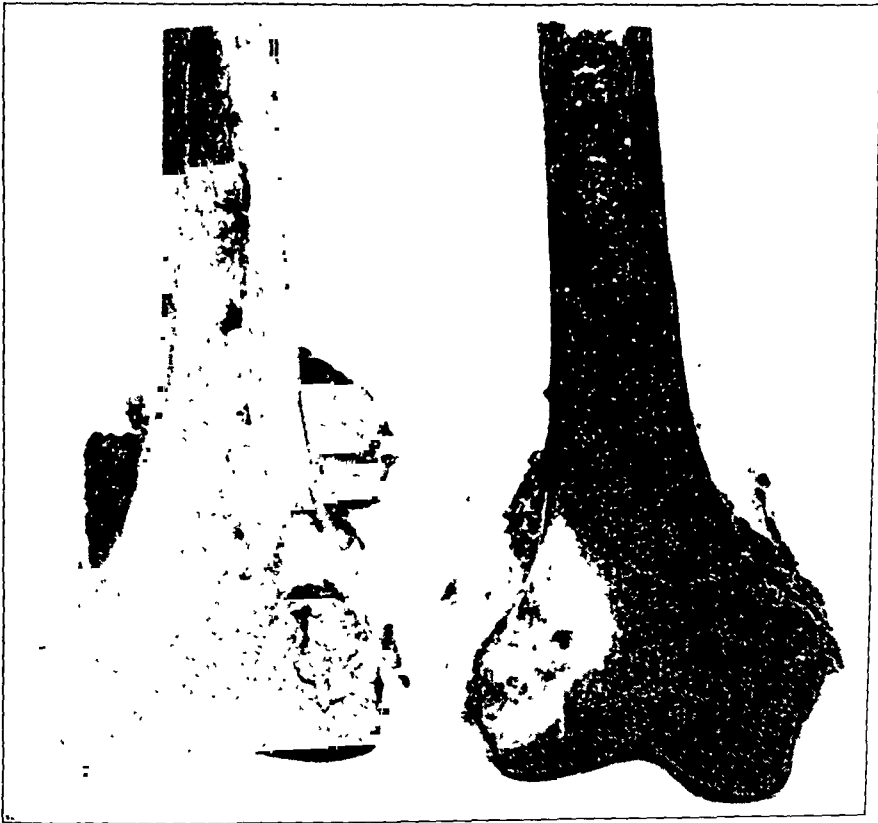


Fig. 59 (no. 20115).—Giant cell tumor of two months' duration in the epiphysis of the femur. Attention is directed to the subcortical location of the lesion and the staining of the surrounding tissue by old blood. The specimen illustrates the typical site of origin of the giant cell tumor.

But this increased osteoclastic activity in an area in which they are already unusually active in the rôle of new bone construction, occurs just at that time when unnourished cortical bone is undergoing necrosis. An imbalance is thus created between bone destruction by osteoclasts and new bone formation that would normally proceed from the reactive cortex were its circulation intact. The defensive reaction of cortical bone, therefore, is suspended while bone destruction by osteoclasts is at its height. This imbalance results in an unchecked hyperplasia of

the osteoclasts and produces a tissue characteristic of giant cell tumor and the early phase of osteitis fibrosa or bone cysts.

In the metaphysis, the reactive cortical bone which is thick and vascular, is apparently capable after a time of overtaking the osteoclasts. In the epiphysis, however, bone destruction seems to proceed at a faster rate than the thin cortical bone in this region can overtake. The result is an arrested lesion or bone cyst in the metaphysis, and a progressive or unchecked lesion in the epiphysis which is known as the giant cell tumor. Even in the epiphysis, however, the balance can be restored if surgical intervention occurs before the bone shell is too extensively destroyed. If the osteoclastic tissue is removed by the curet and cautery (and we suggest by aiding nature to collapse the bone cavity remaining), the giant cell tumor will also go on to ultimate healing.

Thus, histologically, trauma is related to the bone cysts and the giant cell tumor, not as an indefinite etiologic factor but as an initial event in disrupting the cortical blood supply which produces an imbalance between osteoclastic proliferation in the medulla and reactive compact bone in the cortex. In the etiology of these lesions individual variations in collateral circulation as well as the extent of the injury are important factors. That additional metabolic factors may enter into the production of this unbalance is shown by the analysis of multiple giant cell tumor and bone cysts presented in this paper, and the studies by Wilder^{25a} on the serum calcium and phosphorus in these conditions. It is apparent, however, from the studies recorded here that the age of the patient, the site of the injury, the rate and extent of cartilaginous ossification at the end of the bone and the nature of the blood supply in the affected regions are the predominant factors in the pathologic process of bone cysts and giant cell tumors.

When all of these factors are considered, it is apparent why both bone cysts and giant cell tumors are rare in comparison to the frequency of trauma. It must be emphasized that to have the lesions clinically, an imbalance in two normal repair processes is necessary—an unusual increase of osteoclastic proliferation and a diminution or suspension of new bone formation in an injured cortex. These two processes are always active after injury. Both fibro-ostosis (osteitis fibrosa tissue) and osteoclastic proliferation (giant cell tumor tissue) are to be seen after ordinary fractures (fig. 60) and in the healing of a subperiosteal hematoma (Cone⁵²). Only when the bone destructive phase of giant cell proliferation is in the ascendancy for a significant period do the clinical entities of giant cell tumor or osteitis fibrosa arise.

The reasons for the distribution of giant cell tumors and bone cysts in certain favorite localities can now be pointed out. We know that the most frequent site of the solitary bone cyst is in the femur near the great trochanter and in the humerus near the greater tuberosity. These

are points of trauma at the hip and at the shoulder. Bone cysts, rather than giant cell tumors form at these sites because the epiphysis in the head of the femur and the head of the humerus are shielded from trauma and enclosed in the sheltered acetabulum and glenoid cavities. Trauma, therefore, reaches the shaft side of the epiphysis and a more resistant



Fig. 60 (general pathology, no 58) —A healing fracture in a rib of a normal dog. Seven giant cells to the low power field are busy reforming the medullary cavity after callus formation. This illustrates the phase of osteoclastic proliferation in the normal healing process.

and better developed cortex of compact bone arrests these lesions after a time. On the other hand, in the lower end of the femur, the upper end of the tibia and the lower end of the radius, the epiphysis is exposed and

frequent trauma in these localities accounts for the prevalence of giant cell tumors at these points. In the upper end of the tibia, both the epiphysis and metaphysis at the tuberosity of the tibia are exposed to injury, and in this location both giant cell tumor and bone cysts occur. That these regions should be peculiarly susceptible to the trauma received is due to the active state of the bone-forming process in these localities. For, as Poland²⁴ has pointed out, "in the tibia and humerus the upper ends, in the femur and bones of the forearm, the lower ends, are in this respect (bone growth) the most active."

That it is locality alone that accounts for the difference between bone cysts and giant cell tumor can now be more clearly demonstrated. It has been pointed out earlier that the polycystic osteitis fibrosa is an earlier form of bone cyst. The short duration of symptoms, the vascularity and the giant cell areas confirm this. More important still the subcortical location of these lesions demonstrates that they have an identical mode of origin with the giant cell tumor. The infiltration of the giant cell areas by fibro-ostosis shows from the outset that they are destined to be arrested by a restoration of the balance between fibro-ostosis and osteoclastic proliferation.

It is also clear now just how pathologic fracture helps to heal a bone cyst. Not only does such an injury serve to collapse the rigid walls of the cavity, but in the area of shaft bone a fracture serves to reverse the process of circulatory disturbance already described.

The severing of the continuity of the shaft interrupts the medullary circulation and stimulates the periosteal blood supply, at the same time cutting off the nutrition of the osteoclastic tissue which receives blood from the medullary vessels. This process of circulatory changes following fracture has been ably reviewed by Robinson.⁵⁶

Embryonic Histology in Relation to Pathologic Changes.—Since the time of Cohnheim⁵⁷ in 1877, the histogenic relationship of tumor has been inferred and speculated on, much data having accumulated in support of this view. But unfortunately Cohnheim placed emphasis only on the abortive products of embryology—cell rests—rather than on the histogenic processes in themselves. For this reason no painstaking effort to correlate the embryonic histology of the bone with the pathology of the bone tumors has ever been undertaken, to our knowledge. This most fruitful field of investigation has remained practically unexplored.

In advancing the knowledge concerning malignancy no possible realm of information can justifiably be neglected. The facts are many, con-

56. Robinson, W. H.: The Rôle of the Circulation in the Healing of Fractures, *Arch. Surg.* 17:420 (Sept.) 1928.

57. Cohnheim, J.: *Geschwülste, Allgemeine Pathologie*, Berlin, 1877, vol. 1, p. 622.

nections few and hazy. Therefore, the correlation of the more fundamental facts of histogenesis, anatomy and physiology of bone, although difficult, is of first importance to the understanding of tumor formation in these structures. Perhaps at this stage of our knowledge it is even more to be desired than additional points in the clinical history. We have attempted here to bring the pathology into relationship with the more fundamental facts of histogenesis and physiology and to begin the larger undertaking of approaching tumors from this standpoint.

The primitive transformations in skeletal tissue—the stage of cartilaginous calcification, the stage of resorption of substitution bone and the final stage of permanent subperiosteal compact bone all have their corresponding pathologic significance. The function of direct bone formation from fibroblasts to osteoblasts to osteoid tissue, typical of the final stage of bone development, we have found to be instrumental as a healing reaction (fibro-ostosis) in the repair of bone and significant for the understanding of osteitis fibrosa. The function of bone resorption by osteoclasts followed by increased vascularity and the creation of medullary spaces, while a characteristic phase in the histogenesis of bone plays also a fundamental rôle in the production of giant cell tumor. And in the same way, the more primitive histogenic functions underlying the transformation and calcification of cartilage are reproduced in the pathologic process of osteogenic sarcoma. This last carries us into the realm of malignancy and sarcoma. It will form the theme of a subsequent paper.

SUMMARY

In an analysis of over 400 cases of tumors in the giant cell group a pathologic relationship was established between the bone cyst, giant cell tumor of the long bones and skull, giant cell epulis of the alveolar borders and giant cell tumors of the tendon sheaths. The usual bone cyst occurring in the metaphyseal region of the long bones of young patients was shown to be a healing phase of giant cell tumor—a conclusion based on clinical, pathologic and anatomic observations and demonstrated by an analysis of numerous transitional lesions between these two entities.

Giant cell tumors of the skull and long bones, epulides of the alveolar border, and giant cell xanthomas of the tendon sheaths were found to be fundamentally related to a transitional process characterizing the histogenesis of permanent bone, via the indirect route of substitution bone. This transition process underlying all of these tumors, as shown by embryologic studies, involves a proliferation of giant cell osteoclasts, the function of which is to initiate the canalization and vascularization of the preliminary calcified structure.

In the long bones the preliminary calcified structure, is calcified cartilage, and this is resorbed by a proliferation of giant cells in the epiphyseal region—a distortion of this proliferative process leading to giant cell tumor.

In the skull a similar giant cell hyperplasia characterizes certain cartilaginous centers of ossification, and giant cell tumors, it was demonstrated, occur only at such sites in the portions of the skull derived from cartilage and not in the membranous bones.

In epulides of the alveolar border, the temporary calcified structures are the roots of the deciduous teeth, about which giant cell odontoclasts proliferate, attacking the cementum to bring about shedding of these deciduous structures. Here again this normal giant cell proliferation forms the basis for giant cell tumors at these sites resulting in the epulis of the alveolar border.

In the so-called xanthomas of the tendon sheaths containing giant cells, the initial calcified structures are the sesamoid bones derived from fibrocartilage, and giant cell tumors of the tendon sheaths were shown to arise only at the sites in which these small bones are implanted in the tendons.

Evidence was advanced to show that the factor superimposed on this most important transitional giant cell proliferation, necessary to the production of giant cell tumor, was a disturbance of the vascular supply to these regions following trauma. But in each instance, the underlying normal histogenic function of giant cell proliferation was stressed as the essential factor, and it was pointed out that this histogenic basis necessitates the view that giant cell tumors are neoplastic and not inflammatory in origin. The importance of this histogenic conception for the analysis of other tumors was also emphasized.

THE RELATION OF THE ADRENAL GLAND TO THE TOXEMIA OF INTESTINAL OBSTRUCTION

AN EXPERIMENTAL STUDY *

R. A. CUTTING, M.D., PH.D.

NEW ORLEANS

A rather considerable volume of experimental and controversial literature on the general subject of intestinal obstruction has appeared within recent years and has served to focus the interest of the surgeon on this interesting, and often most trying, condition. Much of interest has apparently been demonstrated as to both pathology and treatment, considerably more has been surmised and hypothecated, and still more is as yet unknown. From a practical point of view the alkalosis and dehydration which occur, particularly in so-called "high intestinal obstruction," and the diminished chloride content of the blood plasma, have served as valuable points of departure for therapeutic measures, but rather obviously the correction of such abnormalities partakes of the nature of symptomatic rather than curative treatment. The treatment for certain types of obstruction by the administration of spinal anesthesia has been successfully used by many clinicians, especially in the European clinics, and is rational in that such anesthesia may be made to ascend sufficiently high to block the inhibitor control pathway to the intestine by way of the white rami communicantes and thus prevent inhibitor impulses from spreading to the splanchnic nerves, a procedure which amounts to an actual reinforcement of the motor impulses which are normally continually reaching the intestine through the motor, or vagus, nerve supply; experimentally, the correctness of this line of reasoning has been partly, at least, substantiated by the observation that splanchnic anesthesia does actually tend to overcome obstruction by increasing the number and force of peristaltic contractions. However, even the restoration of normal motor power to the wall of the intestine apparently somewhat misses the mark, for a relatively tremendous number of experimental observations have accumulated which seem to demonstrate conclusively that the essential feature in obstruction is toxemia, particularly in those types of obstruction in which there is production of a closed loop or loops or in which strangulation occurs.

Since the latter types of ileus afford the most acute problem for the clinician, and since mild toxemia is almost undoubtedly a feature of the simplest of cases, the crux of the entire mechanism of intestinal obstruc-

* Submitted for publication, March 16, 1929.

* From the Department of Surgery, Tulane Medical School, Tulane University.

tion, from the clinical point of view at least, seems to be the source, mode of production, action, nature and neutralization of the offending toxin. Any extended study of the literature on this problem carries one through a veritable maze of observations unrelated or only partly correlated at present, some of which are actually contradictory and none of which in the present state of information gives immediate promise of a complete solution of the problem. Such theories as have been advanced are only partly explanatory and are largely at variance one with another.

In general, the only definite conclusions that appear to have been reached at present are that a toxin seems to develop in the lumen and possibly also in the wall of loops of intestine proximal to an obstruction, that this toxin probably is absorbed into the blood stream, and that it is most probably responsible for the toxemia.

The presence of such a toxin has apparently been demonstrated by a number of independent investigators. Murphy and Vincent,¹ Murphy and Brooks,² and Copher and Brooks³ used the fluid contents of the lumen of the intestine above an obstruction virtually unchanged, simply putting it through a strainer or diluting it with water; the toxicity of such a fecal infusion, when injected, would scarcely seem to afford grounds for surprise, in view of its almost certain bacterial contamination. Dragstedt, Dragstedt and Chase⁴ went a step further in that they strained and partially sterilized such fluid prior to injection by heating it to a temperature of 70 C. for an hour, and they further purified it by filtering away the coagulum thus formed; sterility was preserved with chloroform and toluene which in turn were removed, prior to actual injection, by means of heat and filtration. Clairmont and Ranzi⁵ accomplished sterilization by a process of filtration through a Chamberland filter. Stone, Bernheim and Whipple⁶ and Whipple, Cooke and Stearns⁷

1. Murphy, F. T., and Vincent, Beth: An Experimental Study on the Cause of Death in Intestinal Obstruction, Boston M. & S. J. **165**:684, 1911.

2. Murphy, F. T., and Brooks, B.: Intestinal Obstruction: An Experimental Study of the Cause of Symptoms and Death, Arch. Int. Med. **15**:392 (March) 1915.

3. Copher, G. H., and Brooks, B.: Intestinal Obstruction: An Experimental Study of the Therapeutic Value of the Administration of Sodium Chloride, Ann. Surg. **78**:755, 1923.

4. Dragstedt, C. A.; Dragstedt, L. R., and Chase, C. S.: The Antigenic Property of Closed Intestinal Loop Fluid, Am. J. Physiol. **46**:366, 1918.

5. Clairmont, P., and Ranzi, E.: Zur Frage der autointoxication bei ileus, Arch. f. klin. Chir. **73**:698, 1904.

6. Stone, H. B.; Bernheim, B. M., and Whipple, G. K.: Intestinal Obstruction: A Study of the Toxic Factors, Bull. Johns Hopkins Hosp. **23**:159, 1912.

7. Whipple, G. H.; Cooke, J. V., and Stearns, T.: Proteose Intoxication and Injury of Body Protein: II. Metabolism of Dogs with Duodenal Obstruction and Isolated Loops, J. Exper. Med. **25**:479, 1917.

used the fluid contents either after heating to 60 C. for several hours, centrifugating and filtrating it, or after a process of autolysis in the presence of chloroform and toluene for a period of several days. Davis and Morgan⁸ used both the mucosa of the intestine and its contents and prepared a toxin from these substances by admixture with sodium chloride in isotonic solution, addition of toluene and chloroform, autolysis at 37 C. for from two to ten days, heating to 60 C. for thirty minutes, centrifugation and final filtration.

In addition to the foregoing methods for the preparation of toxin, which are admittedly unsatisfactory in that a conglomeration of substances other than the actual toxic principle specifically sought must have been present in all of the products thereby obtained, two noteworthy attempts have been made to prepare the toxic agent in relatively pure form.

J. W. Ellis⁹ described a method of preparing such a toxin by which he believed he had been able to obtain a relatively pure product; he considered this toxin directly responsible for the clinical observations in cases of ileus. He described the preparation of the toxin by the following steps: (1) the collection of the contents and mucosa of the intestine in 250 cc. of hot water; (2) thorough mixing and straining of this material through gauze; (3) the addition of five volumes of 90 per cent ethyl alcohol and subsequent filtration; (4) the boiling of the filtered precipitate with 100 cc. of distilled water; (5) the addition of 1 Gm. of magnesium sulphate after boiling away all traces of the alcohol left in the filtered precipitate, and the continuation of the boiling for a few minutes; (6) filtration, and the precipitation of the filtrate in five volumes of 90 per cent ethyl alcohol; (7) the filtration of this material and the drying of it in a desiccator, and (8) the dissolving, before use, of this material in from 25 to 50 cc. of water and subsequent dialyzation of this solution against distilled water for two hours.

Sugito¹⁰ carried the process a step further, and was able to isolate a supposedly pure toxin not only from the mucosa and intestinal contents, but also from the blood serum of animals with intestinal obstruction. His process of preparation of such a toxin from serum (which is virtually the same as he used in preparing toxin from intestinal loops) consists of (1) heating the latter in boiling water until coagulation takes place; (2) cooling and incubating at 38 C. with an aqueous solution of trypsin and a small amount of toluene until complete digestion of the

8. Davis, D. M., and Morgan, H. S.: Natural Immunity of Animals Against Poison of Intestinal Obstruction, *Bull. Johns Hopkins Hosp.* **25**:39, 1914.

9. Ellis, J. W.: Cause of Death in High Intestinal Obstruction, *Ann. Surg.* **75**:429, 1922.

10. Sugito, S.: Ueber die Todenursache bei Ileus, *Mitt. a. d. med. Fak. d. k. Univ. Kyushu., Fukuoka* **9**:229, 1924.

coagulum has occurred; (3) filtration, coagulation in boiling water and refiltration; (4) addition of one and one-half volumes of saturated magnesium sulphate; (5) filtration through heavy filter paper; (6) solution of the collected precipitate in water and dialyzation in a collodion tube to remove the ammonium sulphate, (7) and reprecipitation with five volumes of alcohol.

There seems to be a general agreement among all the investigators who have worked on the preparation of toxin from the intestinal contents of animals with obstruction that a substance can be prepared relatively easily from such contents which is not present in the contents of normal intestine, which presents fairly definite physical and chemical properties and which, when injected, preferably intravenously, into normal animals, is capable of producing a clinical picture similar to the general clinical picture of intestinal obstruction itself, and ultimately death.

The toxic principle under discussion has been shown to possess the following properties concerning which most investigators are in agreement: 1. It is soluble in water. 2. It is not destroyed by boiling. 3. It is precipitated by five volumes of alcohol and by about 60 per cent ammonium sulphate. 4. It is not destroyed by pancreatic digestion for several days. 5. It does not pass through a collodion membrane when dialyzed against distilled water. Other properties have been described, but many of them either have not been sufficiently substantiated or seem in the present state of knowledge to be of no special significance. The properties mentioned are not, of course, sufficiently definite to establish with certainty either the exact substance or even the general class of substances to which the toxin belongs. Most investigators incline toward the opinion that it is a protein split-product; Stone, Bernheim and Whipple¹¹ and Whipple, Rodenbaugh and Kilgore¹² expressed the belief that it is a proteose; Wilkie¹³ agreed with this idea; Stone¹⁴ and Gerard¹⁵ believed it to be a histamine or histamine-like substance; Ingvaldsen, Whipple, Bauman and Smith,¹⁶ after careful analysis, came to the conclusion that it is a nucleoprotein. Other suggestions which have

11. Stone, H. B.; Bernheim, B. M., and Whipple, G. K.: *The Experimental Study of Intestinal Obstruction*, *Ann. Surg.* **59**:714, 1914.

12. Whipple, G. H.; Rodenbaugh, F. H., and Kilgore, A. R.: *Proteose Intoxication*, *J. Exper. Med.* **23**:123, 1916.

13. Wilkie, D. P. D.: *Acute Intestinal Obstruction*, *Lancet* **1**:1135, 1922.

14. Stone, H. B.: *The Toxic Agents Developed in the Course of Acute Intestinal Obstruction and Their Action*, *Surg. Gynec. Obst.* **32**:415, 1921.

15. Gerard, R. W.: *The Lethal Agent in Acute Intestinal Obstruction*, *J. A. M. A.* **79**:1581 (Nov. 24) 1924.

16. Ingvaldsen, T.; Whipple, A. O.; Bauman, L., and Smith, B. C.: *The Role of Anhydremia and the Nature of the Toxin in Intestinal Obstruction*, *J. Exper. Med.* **39**:117, 1924.

been made are that it is trypsin, a toxic amine, a bacterial exotoxin, an endocrine secretion similar to the parathyroid hormone, cholin, an alkaloid or a ptomaine.

When injected, a toxin prepared according to any of the methods previously described produces a typical picture which includes vomiting, tenesmus, diarrhea, dilatation of the pupils of the eyes, tremor, weakness in the hind legs, weak, rapid pulse, decreased blood pressure and, in fatal cases, death in a state of coma—a picture, as previously mentioned, that corresponds reasonably closely with the clinical picture of experimentally produced ileus.

OUTLINE OF THE PROBLEM

During the course of some experiments on ileus previously reported, I had occasion numerous times in the last several months to employ especially the methods of Ellis and of Sugito in the preparation of toxin in both rabbits and dogs, and my results in general were strictly in accord with the published results of these investigators. However, I have never been able by chemical means to isolate from the blood serum of these animals a toxin by the methods outlined by Sugito, which, when injected into normal animals, would cause their death, although I have made many attempts. Failure to accomplish this was first attributed to the rather inexplicit directions given by Sugito for deriving the substance, but after having devoted considerable time and attention to the matter and after trying many different variations of chemical technic, the statement made by Sugito with reference to his own work with the method that, in spite of the fact that he had derived his toxin from relatively large animals, he had been able to produce death only in very small ones began to acquire considerable significance as offering a fairly obvious explanation for previous failure. Reflection on these facts gradually crystallized itself into two correlative propositions: (1) either so much of the toxin must have been lost during the process of chemical preparation that the amount finally recovered was insufficient to kill animals of anywhere near comparable size, or (2) as the result of the action of the toxin in the animal with intestinal obstruction extending over some considerable period of time, certain organic changes of an undetermined nature must have so debilitated the animal that an amount of toxin sufficient either to kill it or at least to bring it to the agonal state was insufficient to kill another animal of reasonable size.

At about the same time that attempts to prepare toxin from obstructed loops of intestine had been begun, routine histologic examinations of organs of a considerable number of animals dying from the effects of obstruction were studied, and this procedure seemed fairly definitely to demonstrate that characteristic degenerative changes usually occur in the adrenal glands of such animals. Of course, the general

protective function of the adrenal glands has been recognized for a number of years. Boinet,¹⁷ in 1896 and 1897, was apparently the first to observe that animals which had undergone double adrenalectomy were more sensitive to toxic substances than normal animals, and this pioneer work has received confirmation at the hands of many more recent observers. Scott¹⁸ showed that the resistance of adrenalectomized rats to morphine, killed bacteria, and histamine was greatly reduced; Marine¹⁹ and Jaffe showed the same for standard typhoid vaccine; Belding and Wyman²⁰ for diphtheria toxin, and Crivellari²¹ for potassium cyanide, nicotine, acetonitrile and histamine. Lewis²² showed decreased resistance of adrenalectomized animals for cobra venom, curare, veratrine and morphine.

Accordingly, the problem of ascertaining the possible rôle of the adrenal glands in protecting the body economy against the toxin of intestinal obstruction was not far to seek.

OUTLINE OF THE EXPERIMENTS

The experiments that I am about to detail concern themselves with this problem. The general method was the obvious one adopted by the authors mentioned latterly in their investigation of the protective mechanism of the adrenal glands against the various other toxins enumerated. A series of animals was prepared by double adrenalectomy. A similar series of normal ones was used as controls. Half the toxin derived from the intestinal contents and mucosa of an animal with artificial obstruction was injected into an animal in the adrenalectomized series, and the other half into a corresponding animal in the normal series. The animals in both series were kept under observation until death or until the effect of the toxin had disappeared.

(a) *Selection of Animals.*—Only two of the ordinary laboratory animals are available for experiments involving survival after double adrenalectomy, the rat and the rabbit, since these are the only common laboratory animals that survive the operation of double adrenalectomy for any considerable length of time. Furthermore, since the preparation of toxin from obstructed loops of intestine involves

17. Boinet, E.: Diminution de résistance des rats doublement décapsules à l'action toxique de divers substances, *Compt. rend. Soc. de biol.* **49**:466, 1897.

18. Scott, W. J. M.: Influence of Adrenal Glands on Resistance; Susceptibility of Adrenalectomized Rats to Morphine, *J. Exper. Med.* **38**:543, 1923; Influence of Adrenal Glands on Resistance; Toxic Effect of Killed Bacteria in Adrenalectomized Rats, *ibid.* **39**:457, 1924; Influence of Adrenal Glands on Resistance; Susceptibility to Histamine as Test of Adrenal Deficiency, *ibid.* **47**:185, 1928.

19. Marine, D., and Baumann, E. J.: Duration of Life After Suprarenalectomy; an Attempt to Prolong it by Injection of Solution Containing Sodium Salts, Glucose and Glycerol, *Am. J. Physiol.* **81**:86, 1927.

20. Belding, D. L., and Wyman, L. C.: Rôle of Suprarenal Gland in Natural Resistance of Rat to Diphtheric Toxin, *Am. J. Physiol.* **78**:50, 1926.

21. Crivellari, C. A.: Sensitiveness of Adrenalectomized Rats to Certain Toxic Substances, *Am. J. Physiol.* **81**:414, 1927.

22. Lewis, J. T.: Sensibilité des rats privés de surrénales envers les toxiques, *Compt. rend. de l. Séances Soc. de Biol.*, Jan. 22, 1921.

the use of chemical methods, it is readily apparent that the larger the amount of material available at the beginning of the process of preparation, the more likely does the obtaining of a suitable amount of the final product become. Also, it seemed highly desirable to use the same animals for the production of the toxin as for the reception of it by injection. For these reasons, it seemed desirable

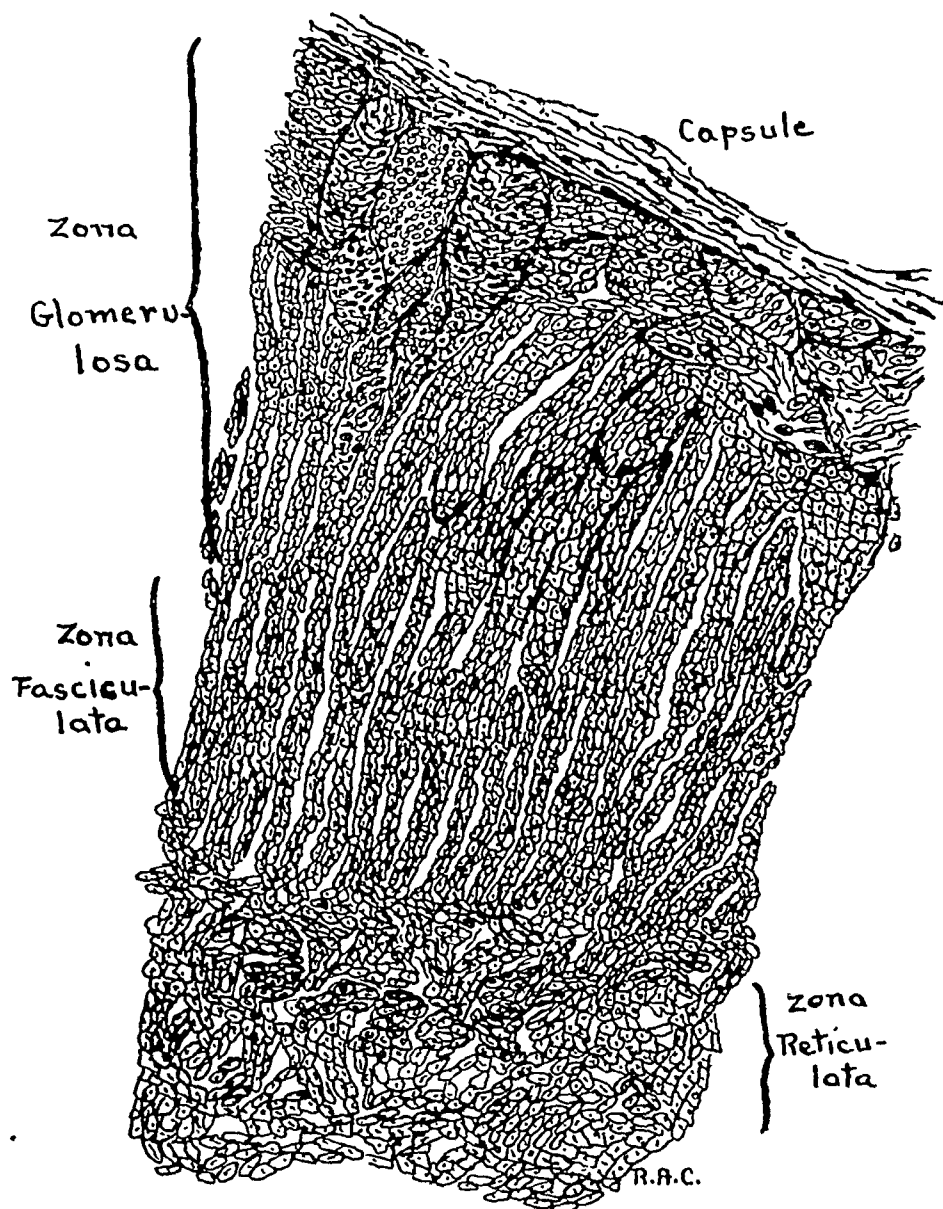


Fig. 1.—Normal suprarenal cortex in the dog; low power sketch.

to use the larger animal, that is, the rabbit. Rabbits weighing from 1 to 1.5 Kg. were obtained.

(b) *Technic of Obstruction and Preparation of Toxin.*—Intestinal obstruction was produced in these animals by tying a piece of ordinary cotton tape tightly about the terminal part of the small bowel, under ether anesthesia, under

strictly aseptic conditions, and with the usual surgical technic. Animals thus prepared were returned to their cages and were kept until they became virtually moribund. It was soon found that animals thus treated survived rarely for much longer periods than forty-eight hours, and this was the time limit maintained for killing them preliminary to the preparation of toxin from their obstructed intestinal lumina. The animals were killed, the entire small intestine above the point of

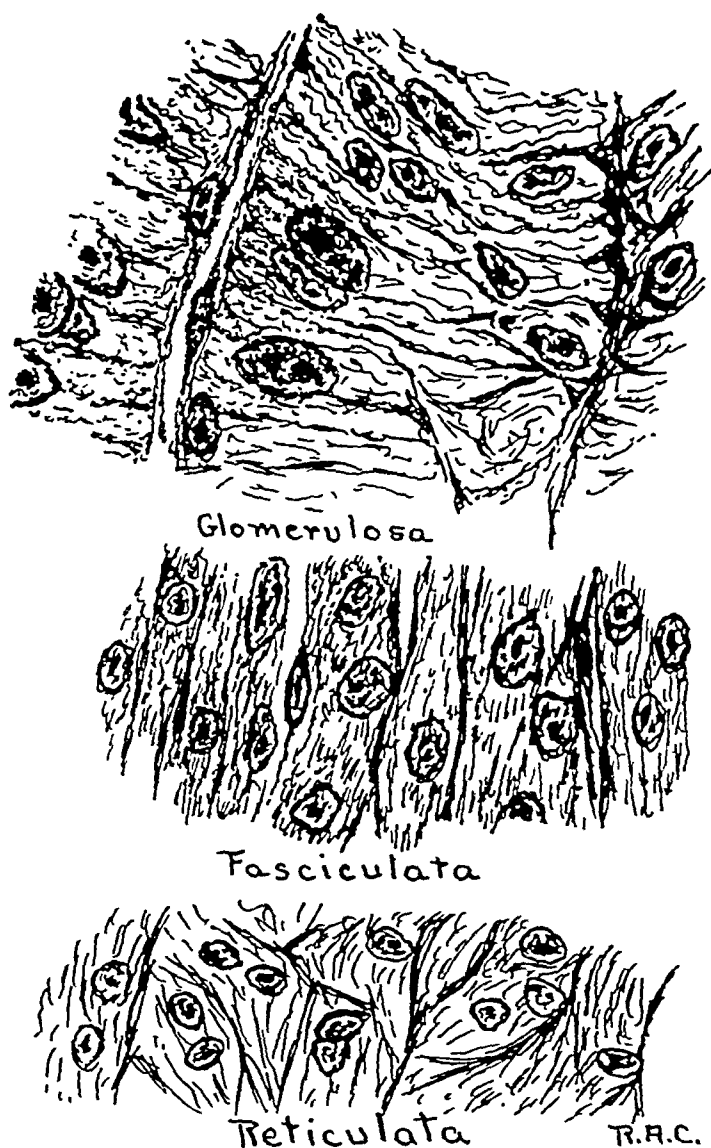


Fig. 2.—Normal suprarenal cortex in the dog; high power sketch.

obstruction up to the pylorus of the stomach being excised in one piece immediately after the production of death by an overdose of ether. The mucosa and contents were removed and this material was placed in a mortar; a small quantity of clean sand was added, and the entire mass was thoroughly rubbed up and macerated with a pestle. This mass was then extracted with water, precipitated with alcohol, and otherwise prepared according to the method of J. W. Ellis, except that, because

of the relatively small amount of material, 100 cc. of water instead of 250 cc. was used for the initial extraction, and correspondingly smaller amounts of the various other ingredients during the course of the preparation.

(c) *Preparation of the Doubly Adrenalectomized Series.*—Animals were prepared for the injection of this toxin by double adrenalectomy, the adrenals being removed by the posterior or kidney route, great care being taken to remove both glands intact in every case. Prior to the injection of the toxin, adrenalectomized rabbits were allowed to survive for a period of two or three weeks, in order that they might fully recover from the effects of the operation and that any abnormalities following the injection of the toxin might reasonably be interpreted as due to it and not to any factor directly associated with the technic of the operation. No attempts were made to select rabbits with any particular care, either for the production of obstruction or in the case of the double adrenalectomy preparation.

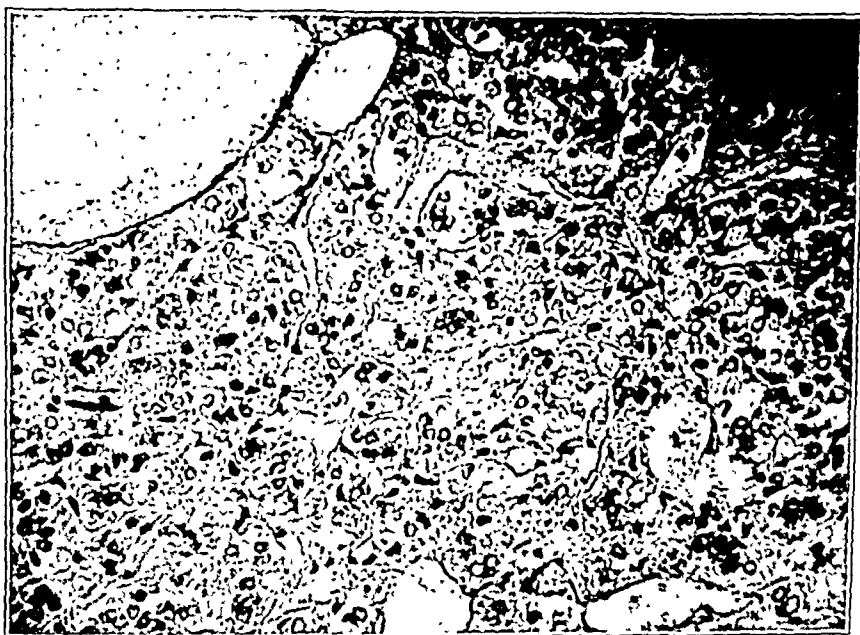


Fig. 3.—Adrenal medulla in the dog following the production of ileus; low power photomicrograph, showing blood vessel dilatation and pseudo clot formation.

The rabbits were fairly large, weighing from 1 to 1.5 Kg. apiece. Some of them were angora, some were ordinary albino rabbits, while others were gray or yellow, many of them being piebald. During the course of the experiment no particular effort was made to control the diet of the animals; this consisted in all cases of bread and lettuce and as much water as the rabbit desired, together with grain in the form of oats.

Twenty-six rabbits were adrenalectomized during the course of the experiment, and of these only six survived the performance of the operation for a suitable length of time.

DOUBLE ADRENALECTOMY

Rabbit 1.—An albino female rabbit weighing 1.6 Kg. was operated on on Aug. 22, 1928. The operation was started at 2 p. m., and completed at 2:35 p. m. There was considerable hemorrhage. The animal reacted from the anesthetic, but died at 3:30 p. m. of hemorrhage.

RABBIT 2.—A piebald female rabbit weighing 1.5 Kg. was operated on on Aug. 22, 1928. The operation was started at 3:05 p. m. and completed at 3:50 p. m. There was considerable hemorrhage. The animal did not react from the anesthetic, and died at 3:55 p. m.

RABBIT 3.—An albino male rabbit weighing 1.1 Kg. was operated on on Aug. 22, 1928. The operation was started at 4:22 p. m. and completed at 4:40 p. m., and the rabbit was returned to his cage in apparently good condition. At 6:30 p. m., however, it was found dead. Autopsy showed the cause of death to be hemorrhage.

RABBIT 4.—A piebald male rabbit weighing 1.4 Kg. was operated on on Aug. 22, 1928. The operation was started at 4:55 p. m., and the animal was returned to his cage at 5:34 p. m. It reacted from the anesthetic, but died at 6:20 p. m. Autopsy failed to reveal the cause of death (insufficiency?).

RABBIT 5.—An albino female rabbit weighing 1.2 Kg. was operated on on Aug. 24, 1928. The operation was commenced at 2:13 p. m., completed at 2:52 p. m., and the animal was returned to its cage apparently in good condition. It reacted from the anesthetic, walked about the cage, and survived for the remainder of the afternoon, but was found dead the following morning. Autopsy failed to reveal the cause of death (insufficiency?).

RABBIT 6.—An albino female rabbit weighing 1.2 Kg. was operated on on Aug. 24, 1928. The operation was commenced at 4:22 p. m. The adrenals were fragmented during the course of the operation, and there was considerable hemorrhage. The operation was completed, and the animal was returned to its cage about 4:52 p. m. It was found dead at 5:28 p. m. Autopsy revealed the probable cause of death as hemorrhage.

RABBIT 7.—An albino female rabbit weighing 1.4 Kg. was operated on on Aug. 24, 1928. The operation was begun at 5:01 p. m. The adrenals were fragmented during the process of removal and considerable hemorrhage was encountered. The animal was returned to its cage at 5:38 p. m. apparently in a moribund condition; it survived only a few minutes. Autopsy revealed the probable cause of death as hemorrhage.

RABBIT 8.—An albino female rabbit weighing 1.4 Kg. was operated on on Sept. 17, 1928. The operation was begun at 2:52 p. m. The adrenals were both removed intact without hemorrhage. The operation was completed, and the rabbit was returned to its cage at 3:21 p. m. apparently in good condition. It survived throughout the afternoon, but was found dead the following morning. Autopsy failed to reveal the cause of death (insufficiency?).

RABBIT 10.—A piebald female rabbit weighing 1.1 Kg. was operated on on Sept. 17, 1928. The operation was commenced at 3:34 p. m. The adrenals were removed intact and without much hemorrhage. The rabbit was returned to its cage at 4:05 p. m. apparently in good condition. It survived the operation and was the first animal successfully doubly adrenalectomized and used in the series.

RABBIT 11.—An angora albino female rabbit weighing 1.6 Kg. was operated on on Sept. 17, 1928. The operation was commenced at 4:15 p. m. The adrenals were removed intact and without much hemorrhage. The operation was completed, and the animal was returned to its cage in apparently good condition at 4:58 p. m. It survived the afternoon, but was found dead the following morning. Autopsy failed to reveal the cause of death (insufficiency?).

RABBIT 12.—An angora albino female rabbit weighing 1.3 Kg. was operated on on Sept. 18, 1928. The operation was begun at 1 p. m. The adrenals were removed readily and with relatively little hemorrhage. The operation was com-

pleted, and the animal was removed to its cage at 1:28 p. m. It survived the afternoon and the following morning until 11:30 a. m., at which time death occurred. Autopsy revealed no apparent cause for death (insufficiency?).

RABBIT 13.—A white female rabbit weighing 1.3 Kg. was operated on on Sept. 18, 1928. The operation was begun at 1:11 p. m. The adrenals were removed intact with little hemorrhage. The operation was completed, and the animal was removed to its cage at 1:29 p. m. in apparently good condition. It survived and was the second animal used in the experimental series.

RABBIT 14.—A white female rabbit weighing 1.5 Kg. was operated on on Sept. 18, 1928. The operation was started at 1:55 p. m. The adrenals were removed with some difficulty; the left gland was fragmented during removal, and considerable hemorrhage was encountered. The operation was completed, and the

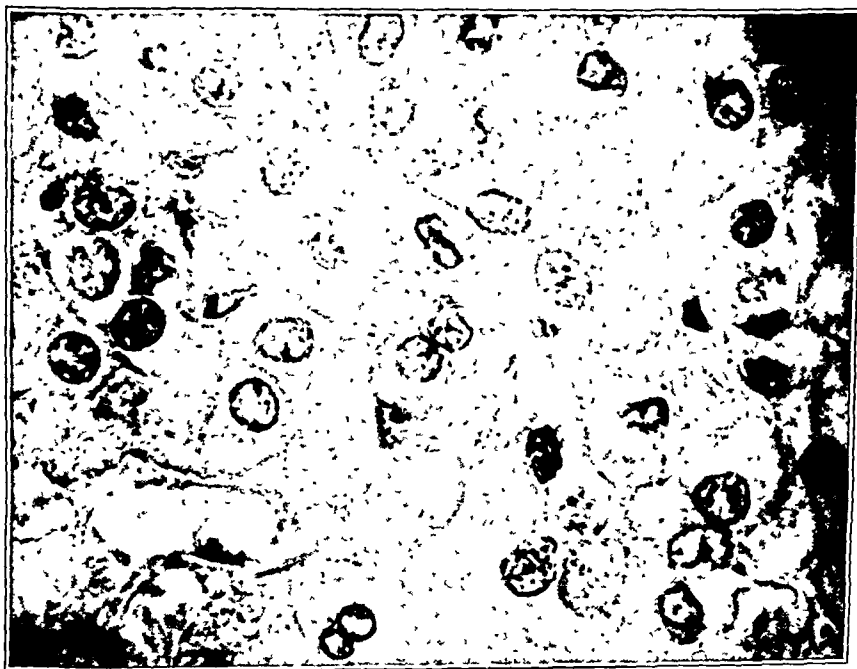


Fig. 4.—Normal adrenal medulla in the dog; high power photomicrograph.

rabbit was removed to its cage at 2:32 p. m. It survived the afternoon, but was found dead the following morning; autopsy showed the cause of death as hemorrhage.

RABBIT 15.—A brown female rabbit weighing 1.1 Kg. was operated on on Sept. 18, 1928. The operation was commenced at 2:50 p. m. Adrenalectomy was performed with little difficulty and with virtually no hemorrhage. The animal was returned to its cage at 3:12 p. m. in apparently good condition. Death occurred at 5:30 p. m.; at autopsy, no cause for death could be discovered (insufficiency?).

RABBIT 16.—A piebald female rabbit weighing 1 Kg. was operated on on Sept. 18, 1928. The operation was begun at 3:35 p. m. The adrenals were removed easily and with little hemorrhage. The animal was returned to its cage at 4 p. m. in apparently good condition. It survived the afternoon, but was found dead the following morning; autopsy failed to reveal the cause of death (insufficiency?).

RABBIT 17.—A piebald male rabbit weighing 1.4 Kg. was operated on on Sept. 19, 1928. The operation was begun at 1:28 p. m. Adrenalectomy was performed with facility and without much hemorrhage. The animal was returned to its cage. It survived and was the third animal used in the experimental series.

RABBIT 18.—A white angora male rabbit weighing 1.2 Kg. was operated on on Sept. 19, 1928. The operation was commenced at 2:11 p. m. The adrenals were removed with some difficulty, both being fragmented and considerable hemorrhage being encountered. The operation was completed and the animal removed to its cage at 2:41 p. m. in relatively poor condition. It died at 4 p. m.; autopsy revealed the probable cause of death as hemorrhage.

RABBIT 19.—A white female rabbit weighing 1.5 Kg. was operated on on Sept. 19, 1928. The operation was begun at 2:45 p. m. Adrenalectomy was unusually easy and relatively little hemorrhage was encountered. The operation was completed, and the animal was removed to its cage at 3 p. m. in excellent condition. It survived the night, but died at 10 a. m. the following morning. Autopsy failed to reveal the cause of death (insufficiency?).

RABBIT 20.—A piebald male rabbit weighing 1.3 Kg. was operated on on Sept. 19, 1928. The operation was begun at 3:05 p. m. The adrenals were removed intact without difficulty and without hemorrhage. The operation was completed, and the animal was removed to its cage at 3:20 p. m. It survived the operation and was the fourth animal used in the experimental series.

RABBIT 21.—A white female rabbit weighing 1 Kg. was operated on on Sept. 21, 1928. The operation was commenced at 2 p. m. The adrenals were removed with some difficulty but without much hemorrhage. The operation was completed at 2:35 p. m., and the animal was returned to its cage in fair condition. It died at 7 p. m.; autopsy revealed no apparent cause for death (insufficiency?).

RABBIT 22.—A white male rabbit weighing 1.5 Kg. was operated on on Sept. 21, 1928. The operation was begun at 2:51 p. m. The adrenals were removed intact with slight hemorrhage. The operation was completed, and the animal was removed to its cage at 3:15 p. m. in good condition. It survived and was the fifth animal used in the experimental series.

RABBIT 23.—A piebald female rabbit weighing 1.1 Kg. was operated on on Sept. 21, 1928. The operation was begun at 3:30 p. m. The adrenals were removed fairly easily but some hemorrhage resulted. The operation was completed at 3:50 p. m., and the animal was removed to its cage. It survived the afternoon, but was found dead the following morning; autopsy failed to reveal the cause of death (insufficiency?).

RABBIT 24.—A white angora female rabbit weighing 1 Kg. was operated on on Sept. 21, 1928. The operation was begun at 4:11 p. m. The adrenals were removed with some difficulty and slight hemorrhage. The operation was completed at 4:31 p. m., and the animal was removed to its cage in fair condition. It died at 5 p. m. apparently of shock; autopsy failed to reveal the cause of death.

RABBIT 25.—A white female rabbit weighing 1.2 Kg. was operated on on Sept. 21, 1928. The operation was begun at 4:45 p. m. Adrenalectomy was difficult and both glands fragmented; there was considerable hemorrhage. The operation was completed, and the animal was removed to its cage at 5:10 p. m. It survived the afternoon, but was found dead the following morning. Autopsy failed to reveal the cause of death (insufficiency?).

RABBIT 26.—A brown male rabbit weighing 1.4 Kg. was operated on on Sept. 25, 1928. The operation was commenced at 2:25 p. m. Adrenalectomy was

accomplished fairly easily, and not much hemorrhage was encountered. The operation was completed at 2:40 p. m., and the animal was removed to its cage. It survived and was the sixth animal used in the experimental series.

THE OBSTRUCTION AND INJECTION SERIES: THE EXPERIMENT PROPER

I. RABBIT 27.—A white female rabbit weighing 1.2 Kg. was used.

Obstruction was produced on Oct. 7, 1928, at 1:15 p. m. The animal was killed on Oct. 9, at 2 p. m., at which time it appeared ill. In the evening, the entire small intestine was removed and from the mucosa and the contents a toxin was prepared, according to the method of Ellis.



Fig. 5.—Adrenal medulla in the dog following the production of ileus; high power photomicrograph, showing pyknosis of nuclei and plasma cell infiltration.

RABBIT 33.—A brown female rabbit weighing 1.1 Kg. was used. The animal was healthy and normal.

RABBIT 10.—Adrenalectomy was performed on Sept. 17, 1928.

The toxin derived from rabbit 27 was divided into two equal parts (in this case 2.7 cc.); one part was injected into the normal rabbit 33, and the other into the adrenalectomized rabbit 10, at 3:15 p. m.

3:15 to 3:30 p. m.: Neither rabbit exhibited any particular symptoms except that both appeared disinclined to move about, and at the end of this period the healthy rabbit was found to have defecated several round, hard pellets.

3:30 to 4 p. m.: Both rabbits "drooped" considerably. The pupils of both were widely dilated, and the normal animal passed considerable quantities of fecal material which first was formed, though soft, but later became mucoid and watery; toward the last, tenesmus was prominent in this animal. The adrenalectomized animal did not defecate nor exhibit tenesmus; it appeared to have been much

less affected by the injection than the normal and was generally brighter and more attentive to its surroundings.

4 to 4:30 p. m.: During the early part of this period the normal animal looked as if it were about to succumb; it lay on its abdomen with legs stretched out before and behind, continued to purge at intervals, was quite apathetic to its surroundings, and was unable to stand or sit; tremors were noticed in the hind limbs but these did not persist. By the end of the period, however, it appeared much better and was beginning to pull up its legs in an attempt to get to its feet, although its efforts were unsuccessful. The adrenalectomized animal was able to sit up, but appeared sick. Both animals refused food, but toward the end of the period it appeared as if both would survive.

4:30 to 5 p. m.: There was little change in the appearance of either animal though both looked somewhat brighter and at the end of the period both were sitting up. It was decided to discontinue detailed observations at this time, and both were returned to their cages.

6 p. m.: The normal animal had apparently almost recovered; the adrenalectomized one was apathetic, but otherwise exhibited no particular symptoms.

7 p. m.: The normal animal had apparently fully recovered, though possibly was not as active as before the injection. The adrenalectomized animal was stretched out and dead.

The normal animal fully recovered.

Autopsy on the adrenalectomized animal revealed no gross lesions in any of the organs, with the single exception of the small intestine; here, in places, was some hyperemia, and the mucosa was reddened in patches. No adrenal tissue could be discovered after careful search.

II. RABBIT 28.—A piebald female rabbit weighing 1.4 Kg. was used. Obstruction was produced at 2 p. m., on Oct. 11, 1928, and the animal was returned to its cage in good condition. The animal was killed at 2 p. m. on October 13, and the contents and mucosa of the small intestine were used for the preparation of toxin according to the method of Ellis.

RABBIT 34.—A white female rabbit weighing 1.2 Kg. was used. The animal was healthy and normal.

RABBIT 13.—Adrenalectomy was performed on Sept. 18, 1928.

The toxin derived from rabbit 28 was divided into two equal parts (4 cc. each in this case); one part was injected into the normal animal and the other part into the adrenalectomized animal at 5 p. m., on Oct. 14, 1928.

5 to 5:15 p. m.: For the first five minutes neither rabbit appeared to experience any ill effect from the injection. However, at the end of this period the normal rabbit defecated a fairly large amount of normally formed stools, and also urinated. At 5:15, both animals were beginning to become somnolent; they sat huddled up with their eyes closed, and resisted any attempts to change their positions.

5:15 to 5:45 p. m.: During this period both rabbits progressively lost control of both hind legs, and the normal one was unable to bear his weight on his front paws. The normal rabbit purged violently; quantities of partially formed stools and, toward the last, very watery and mucoid motions were noted. The adrenalectomized animal passed a few formed fecal pellets. At 5:45 p. m., the normal rabbit was lying on his side with pupils widely dilated, apparently in a moribund condition. The adrenalectomized animal was in only a slightly better condition; it was able to struggle to maintain its position when disturbed, but could not roll onto his abdomen when turned on its side. Both animals presented slight tremors of the extremities.

5:45 to 6:45 p. m.: The adrenalectomized rabbit progressively became comatose, and died rather unexpectedly in convulsions at 6 p. m. The normal animal gradually regained the use of its limbs and was sitting up at 6:45 p. m.

The normal animal fully recovered.

Autopsy on the adrenalectomized animal revealed no gross lesions; examination of the region of the upper poles of the kidney revealed total absence of adrenal tissue.

III. RABBIT 29.—A white male rabbit weighing 1.5 Kg. was used. Obstruction was produced on Oct. 13 1928, at 3:15 p. m., and the animal was returned to its cage in good condition. The rabbit was killed at 4 p. m., on October 15, and toxin was prepared, as in previous cases.

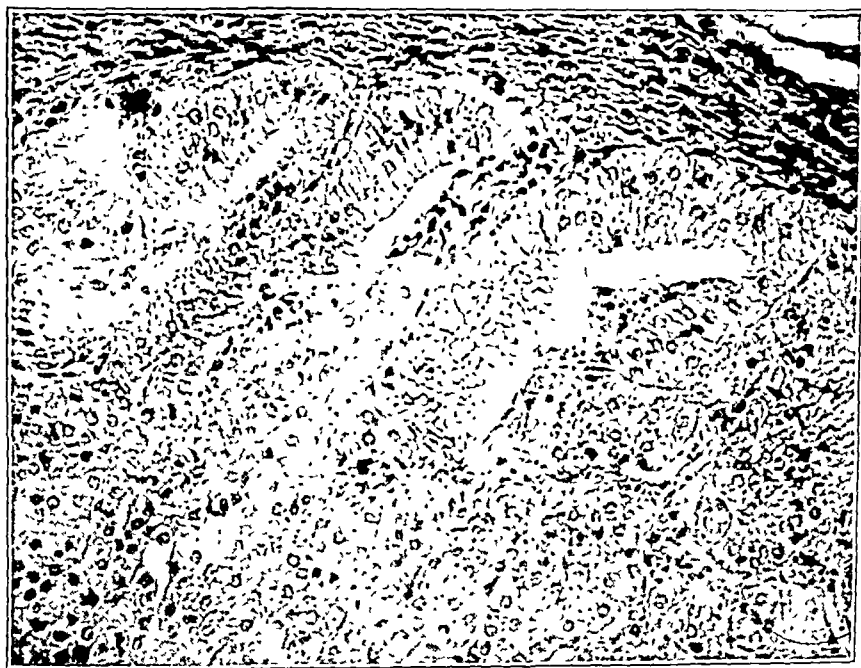


Fig. 6.—Adrenal cortex in the dog following the production of ileus; low power photomicrograph, showing areas of focal necrosis.

RABBIT 35.—A white male rabbit weighing 1.2 Kg. was used. The animal was normal and healthy.

RABBIT 17.—Adrenalectomy was performed on Sept. 19, 1928.

The toxin prepared from rabbit 29 was divided into two equal parts; one part was injected into the normal animal and the other into the adrenalectomized one at 2 p. m. on Oct. 16, 1928.

No special features were noted in this case except that the reaction to the injection was somewhat delayed beyond the intervals previously noted in the case of both rabbits, and neither animal appeared very ill at any time during the first two hours. Both rabbits were returned to their cages at the end of this period with the idea that probably the toxin was relatively inert. In the morning, however, the normal animal was apparently healthy, while the adrenalectomized one was dead. Rigor mortis had become established in the latter animal.

The normal animal survived indefinitely.

Autopsy on the adrenalectomized animal showed no gross lesions of any of the organs. No evidence of adrenal tissue could be found.

IV. RABBIT 30.—A white female rabbit weighing 1.4 Kg. was used. Obstruction was produced on Oct. 14, 1928 at 1 p. m. On October 16, the rabbit was killed and toxin was prepared as in the previous cases.

RABBIT 36.—A brown female rabbit weighing 1.2 Kg. was used. The animal was normal and healthy.

RABBIT 20.—Adrenalectomy was performed on Sept. 19, 1928.

The toxin derived from rabbit 30 was divided into two equal parts (5 cc. in this case); one part was injected into the normal rabbit and the other into the adrenalectomized animal at 2:15 p. m. on Oct. 17, 1928.

The results in this case almost exactly duplicate those reported in the previous case. Both rabbits showed little effect from the injection of the toxin, and were returned to their cages at the end of two hours; the normal animal survived indefinitely, but the adrenalectomized one was found dead on the following morning. The autopsy observations were insignificant except in demonstrating that all adrenal tissue had been removed.

V. RABBIT 31.—A white angora male rabbit weighing 1.3 Kg. was used. Obstruction was produced on Oct. 16, 1928, at 1:30 p. m., and the animal was returned to its cage in good condition. The rabbit was killed on October 18, at 2:25 p. m., and the toxin was prepared as previously.

RABBIT 37.—A piebald male rabbit weighing 1.4 Kg. was used. The animal was healthy and normal.

RABBIT 22.—Adrenalectomy was performed on Sept. 21, 1928.

The toxin derived from rabbit 31 was divided into two equal parts (2.5 cc. in this case); one part was injected into the normal rabbit and the other into the adrenalectomized animal on Oct. 19, 1928, at 3:10 p. m.

3:20 p. m.: The normal rabbit defecated a quantity of soft formed stools; it appeared sick and its respirations and pulse rate were rapid. The adrenalectomized animal was unaffected.

3:30 p. m. The normal animal was weak and had some difficulty in maintaining its balance; the adrenalectomized animal began to look sick.

3:40 p. m.: The normal rabbit had purged violently mucous and watery stools. The adrenalectomized animal had also defecated, but the movements were normal.

4 p. m.: Both rabbits had become so weak that they could no longer stand. The pupils of both were widely dilated; the skins of both were deeply cyanosed. Both exhibited fibrillary twitchings in the rear limbs.

5 p. m.: Both rabbits were in essentially the same condition as previously, except that paralysis was more marked in the adrenalectomized animal.

6 p. m.: Both rabbits were very sick, but the formerly normal one had apparently recovered somewhat. Both were placed in their cages for the night.

8 p. m.: The adrenalectomized animal died in violent convulsions. The normal animal had recovered somewhat.

Two cubic centimeters of blood was taken from the ear veins of both animals for chloride determination just prior to the injection of the toxin and a similar amount at the end of two hours for the same purpose. The chloride determinations showed: in the normal animal prior to injection, 528 mg. per hundred cubic centimeters, while two hours after injection it was 518 mg. per hundred cubic centimeters; in the adrenalectomized animal prior to injection, 445.5 mg. per hundred cubic centimeters, while two hours after injection the amount was the same.

The normal animal survived indefinitely.

Autopsy of the adrenalectomized animal showed absence of all adrenal tissue. No significant organic changes were found, with the exception of moderate distention of the small intestine which was filled with liquid yellow contents and a great deal of mucus.

VI. RABBIT 32.—A white female rabbit weighing 1.5 Kg. was used. Obstruction was produced on Oct. 19, 1928, at 4:20 p. m., and the animal returned to its cage in good condition. The rabbit was killed on October 21, at 5 p. m., and the toxin was prepared as previously.

RABBIT 38.—A piebald female rabbit weighing 1.2 Kg. The animal was healthy and normal.

RABBIT 26.—Adrenalectomy was performed on Sept. 25, 1928.

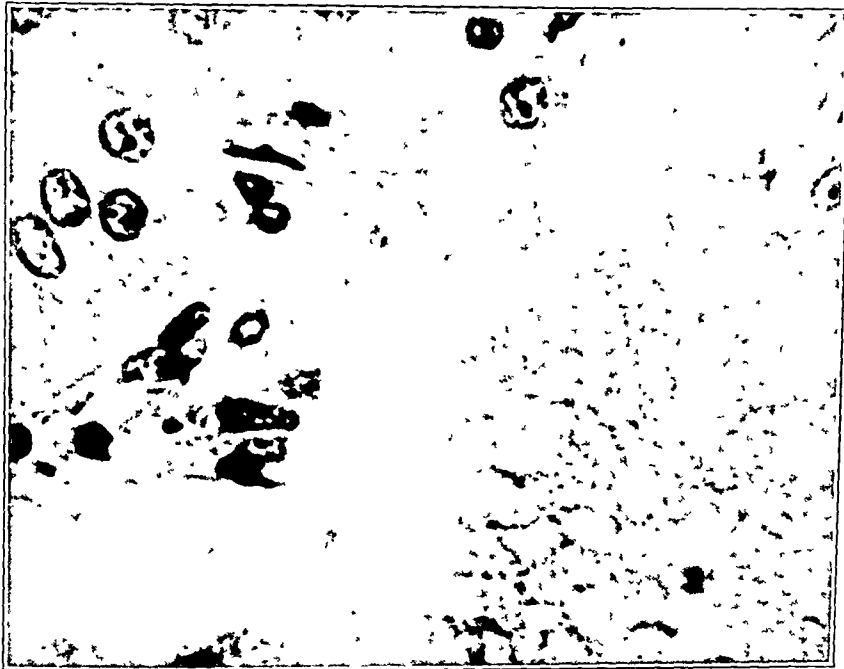


Fig 7.—Adrenal cortex in the dog; high power photomicrograph of figure 6, showing pyknosis of nuclei and part of the area of focal necrosis.

The toxin derived from rabbit 32 was divided into two equal parts (3 cc. in this case); one part was injected into the normal (rabbit 38) the other into the adrenalectomized animal (rabbit 26) at 3:30 p. m. on Oct. 20, 1928.

No particular features of new interest were noted. Both rabbits experienced rather severe reactions within an hour; both became practically comatose in an hour and a half; they both exhibited some tenesmus, but the bowel movements of the normal rabbit were profuse and mucoid, while those of the adrenalectomized rabbit were scanty and formed, though soft and covered with mucus. Both animals were in apparently in extremis at the end of two hours. Two cubic centimeters of blood had been secured from the ear veins of both of the animals for a blood chloride determination just prior to the injection of the toxin. It had been decided to secure a similar amount at the end of two hours, in order that any possible decrease in chlorides might be detected. Both animals, however, were virtually

moribund at the end of two hours, as previously noted, and blood could not be secured from the veins of either animal. It was felt that neither animal could survive many minutes longer, and cardiac puncture was performed.

The adrenalectomized animal died during this procedure, possibly a cardiac death.

The normal animal recovered and survived indefinitely.

Autopsy on the adrenalectomized animal showed no adrenal tissue. The heart showed evidence of puncture, of course, but only a drop or two of blood was found in the pericardium.

The chloride determinations showed: in the normal rabbit before injection, 501.6 mg. per hundred cubic centimeters, and after injection, 495 mg. per hundred cubic centimeters; in the adrenalectomized rabbit before injection, 511.5 mg. per hundred cubic centimeters and after injection, 462 mg. per hundred cubic centimeters

SUMMARY

Under as similar conditions as could well be devised six pairs of rabbits were injected with toxin chemically prepared, in as pure form as possible, from the mucosa and intestinal contents of other rabbits in which obstruction had been present for about forty-eight hours. Each pair of animals that had been given injections of toxin consisted of one rabbit which was healthy and normal, as far as could be determined, and an animal from which both adrenals had been completely removed approximately two or three weeks previously, and which had apparently completely recovered from the effects of the operation. Precisely the same dose of toxin was injected into both animals of each pair, the toxin from one animal with obstruction being divided for the purpose into two equal parts. The weight of the normal animal of each pair was selected so as never to exceed the weight of the adrenalectomized one, thus throwing any possible advantage in favor of the operated animal.

The results were conclusive. Both animals of each pair showed the symptoms of intoxication that have been previously reported by several investigators: weakness, tremors, dilated pupils, diarrhea and tenesmus. The normal rabbits invariably showed much more severe reactions than the adrenalectomized rabbits, and diarrhea with tenesmus was a prominent feature of the intoxication. The adrenalectomized animals showed the latter manifestations in very mild degree. While the animals of the normal series all survived indefinitely, though after a period of alarmingly severe reactions in most cases, the adrenalectomized rabbits all died within a period of twelve hours, in spite of the apparently relative mildness of their reactions.

Blood chloride determinations in two pairs of animals showed either no decrease at all or only slight decrease in chloride content during the two hour period following the injection of the toxin, and while the animal showing the greatest decrease was one from the adrenalectomized series and, accordingly, died, the animal showing the next greatest decrease was a normal animal and lived. Furthermore, the other adrenalectomized

animal showed no decrease, though it died, while the other normal animal showed no significant decrease yet lived.

It is accordingly believed that these experiments demonstrate that:

1. The lethal dose of toxin derived from the mucosa and intestinal contents of animals in which obstruction has been produced is much less for doubly adrenalectomized animals than for normal ones.

2. The adrenal glands evidently serve a definite function in combating a toxemia produced by the injection of toxin so derived.

3. The severity of the symptoms and signs of such a toxemia are a false guide to the prognosis in cases in which the adrenals cannot function.

COMMENT

The present series of experiments will have little interest for those who feel that the characteristic toxin which can be prepared, as previously described, from the contents and mucosa of loops of intestine proximal to an obstruction is an adventitious substance that ordinarily does not find its way into the circulation and therefore has no essential part in the production of the toxemia of ileus. On the other hand, granted that the reverse is true, and that the toxin under discussion probably does enter into the etiology of the symptom complex, a new and most fascinating sidelight is thrown on the problem of intestinal obstruction by the apparent incrimination of the adrenal glands as agents in a protective mechanism against the toxemia. Unfortunately, in spite of the fact that the adrenal glands have been known for years to subserve such a protective mechanism in the case of other toxic substances, organic and inorganic, no effective way of reinforcing this protective action in times of stress and strain has as yet been devised either through the isolation of an efficient and injectable extract of the adrenal gland of other animals or by measures designed to support the gland of the affected animal during the period in which it is called on to carry a load which it cannot bear unaided.

All the evidence at present available seems to indicate that the cortex of the adrenal gland and not the medulla is the tissue responsible for the protective mechanism, but attempts to utilize this fact in a practical way have apparently thus far met with failure. Such cortical extracts as have been prepared have been disappointingly inefficient, although emulsions of cortical tissue have been shown to detoxify at least one biologic toxin (Cobra venom, Meyers²³), and autoplasmic transplantation of the adrenal cortex has been shown to increase the resistance of animals previously lowered by adrenalectomy (Jaffe²⁴).

23. Meyers: Tr. Path. Soc. London, 1898.

24. Jaffe, H. L.: On Diminished Resistance Following Suprarenalectomy in the Rat and the Protection Afforded by Autoplasmic Transplants; Am. J. Path. 2:421, 1926.

On the basis of such fragmentary knowledge as is available at present, it seems probable that the influence of the adrenal cortex in combating intoxication is indirect rather than direct, and possibly a fairly complicated mechanism is involved. Perhaps the adrenals influence the general metabolism or the special metabolism of some intermediate tissue or they may control the usual mechanism of antibody production. In this connection the observation of Marine and Baumann is interesting—that the administration of physiologic solution of sodium chloride and Ringer's solution is of value in prolonging the life of those animals which ordinarily rather quickly succumb after double adrenalectomy, since the administration of sodium chloride is known to be of value in combating the toxemia of intestinal obstruction clinically.

From a clinical point of view it is believed that an appreciation of this protective function of the adrenal glands in intestinal obstruction is of the utmost importance. If, as seems to have been established histologically, these glands undergo degenerative changes in obstruction, it must be fairly obvious that treatment in order to be effective must be instituted early in intestinal obstruction, and such treatment must be aimed at the removal of toxic products from the obstructed loops of intestine before extensive degenerative changes have occurred in the adrenal cortices.

An amount of toxic absorption can be successfully combated by the body in the earlier stages when the adrenal mechanism is intact which would be rapidly and inevitably fatal once the cortical function has been seriously damaged.

Consequently, it would seem irrational to temporize very long with symptomatic treatment in any severe clinical case. The administration of spinal or splanchnic anesthesia in an attempt to relieve an adynamic ileus must be performed early and not as a last resort. In the early stages of obstruction the restoration of the motor function by any means will be effective, since the cortical protective mechanism is intact; later such restoration, though complete, may be just as hopelessly ineffective, since even though further absorption may be minimized or completely overcome, the protective mechanism may be unable to take care of the dose already absorbed.

In a similar way, enterostomy, to be effective, must be performed relatively early. It will almost inevitably allow the escape of only part of the toxic intestinal contents, and the condition of the cortical protective mechanism will determine whether the individual can successfully take care of the residuum or whether he will be overwhelmed thereby.

ACUTE COMPLETE OBSTRUCTION OF THE DUODENUM FOLLOWING A GASTROJEJUNOSTOMY

CURE BY DEGASTRO-ENTEROSTOMY *

JOHN E. SUMMERS, M.D.

OMAHA

The clinical fact has long been noted that the immediate seriousness of an acute intestinal obstruction depends on the location of the obstruction. When located in the duodenum, the higher the obstruction is below the opening through which the bile and pancreatic secretions are discharged, the more serious is the toxicity and the earlier the fatality. Numerous experimental occlusions of the duodenum have proved this.¹ Rapid fatalities follow obstructions in the small intestine, and the nearer the obstruction is located to the approach to the duodenum, the earlier death occurs. On the other hand, obstructions in the large bowel may exist for a considerable number of days before symptoms threatening life develop. Of course, if the obstructing cause, wherever located, so interferes with the vitality of the bowel that the blood supply is shut off, gangrene and peritonitis hasten the end. In such an instance, bacterial infection is overwhelmingly added to the causes of the commonly described toxemia. Not infrequently disorders of general health are noted in incomplete duodenal stenosis, most often located near the duodenojejunal junction.² However much one may agree or disagree with experimental physiologists³ that the chief danger in acute intestinal obstruction is the loss of water and the inorganic constituents of the blood, there is, in my opinion, no question that safety for the sufferer consists primarily in draining the intestine. This, when done early, is accomplished by relieving the obstruction itself. When the patient is not seen until late, only temporizing measures are permissible, and the procedure of a simple drain introduced into the bowel above the obstruction is indicated. It has been proved experimentally and clinically that sodium chloride, when administered, has a positive effect in reducing the toxicity in intestinal obstruction. It is given intravenously, subcutaneously and by rectum, in large quantities of water. The water is

* Submitted for publication, March 5, 1929.

1. Duval, P.; Roux, J. C., and Bécclère, H.: *Études sur le duodénum*, Paris, Masson & Cie, 1924.

2. Summers, J. E.: The Dilated Duodenum, *Ann. Surg.* **88**:576 (Sept.) 1928.

3. Discussion of symposium on Intestinal Obstruction, *J. A. M. A.* **91**:1592 (Nov. 24) 1928.

corrective of the dehydration. If one should await the corrective effects of the toxicity resulting from the intravenous administration of sodium chloride before establishing drainage above the obstruction, I fear it would be bad judgment. The acts of intestinal drainage, intravenous administration of large quantities of physiologic solution of sodium chloride and blood transfusion should go hand in hand—at least that is my experience.

In papers of my own⁴ I have advocated the vital importance of draining the intestine above the obstruction, emptying the intestine through several incisions, when practicable. Forgetting for the moment chloride depletion, Holden⁵ has given the best corroborative evidence that the greatest danger of acute intestinal obstruction, wherever located, may be toxemia from absorption of the intestinal contents. Among his last fifty-one patients with acute intestinal obstruction on whom operations were performed, there were only three deaths, whereas, among a large number on whom operations were done before these his mortality rate was 50 per cent. He attributed his, probably to date unapproached, improved success to the fact that in each instance he practiced a method of emptying the imprisoned intestinal contents by a process of stripping, which caused almost complete emptying.

The foregoing digression from the subject of my clinical report seemed necessary because of the unusual opportunity afforded to discuss the dangers of delay, especially in high intestinal obstruction, as well as the possibilities of sustaining life by the measures advocated by physiologists.

REPORT OF A CASE

A well developed and well nourished man, aged 28, an intern, was admitted as a patient in the University Hospital on Aug. 28, 1927, with the diagnosis of acute appendicitis and duodenal ulcer.

History.—In 1917 had begun a spring and fall series of rather vague gastric discomforts which were relieved by sodium bicarbonate and the taking of food. These symptoms continued, but to a lesser degree, through the patient's premedical course. During the four years of the medical course there was again a feeling of distention and gnawing in the epigastrium about two or three hours after meals. It seemed to be aggravated by acid food and by periods of stress, mental and physical, but had practically no seasonal relationship. Fluoroscopic and roentgen examinations confirmed the clinical diagnosis of duodenal ulcer. The hospital record showed that the young man had the benefit of the modern recognized medical treatment for duodenal ulcer, and that in spite of carrying on his part of an active surgical service he led a relatively comfortable existence, provided he was careful of his diet.

4. Summers, J. E.: *Tr. Sect. Surg. & Anat. A. M. A.*, 1902; *Med. Herald* 25:295, 1904; *Tr. Am. Surg. Ass.*, 1920, p. 377; *Nebraska M. J.* 11:335, 1926.

5. Holden, W. B.: *Intestinal Obstruction: Survey of 135 Personal Cases*, *Arch. Surg.* 13:882 (Dec.) 1926.

The day previous to admission as a patient, he experienced colicky pain and cramps in the right lower quadrant, followed by nausea and vomiting. As there was no apparent urgency about the case—the only physical observations being some muscle spasm tenderness in the right lower quadrant—surgical intervention was delayed.

Operation.—On Sept 5, 1927, with the patient under general anesthesia, a high right rectal incision exposed the stomach and an area of induration near the

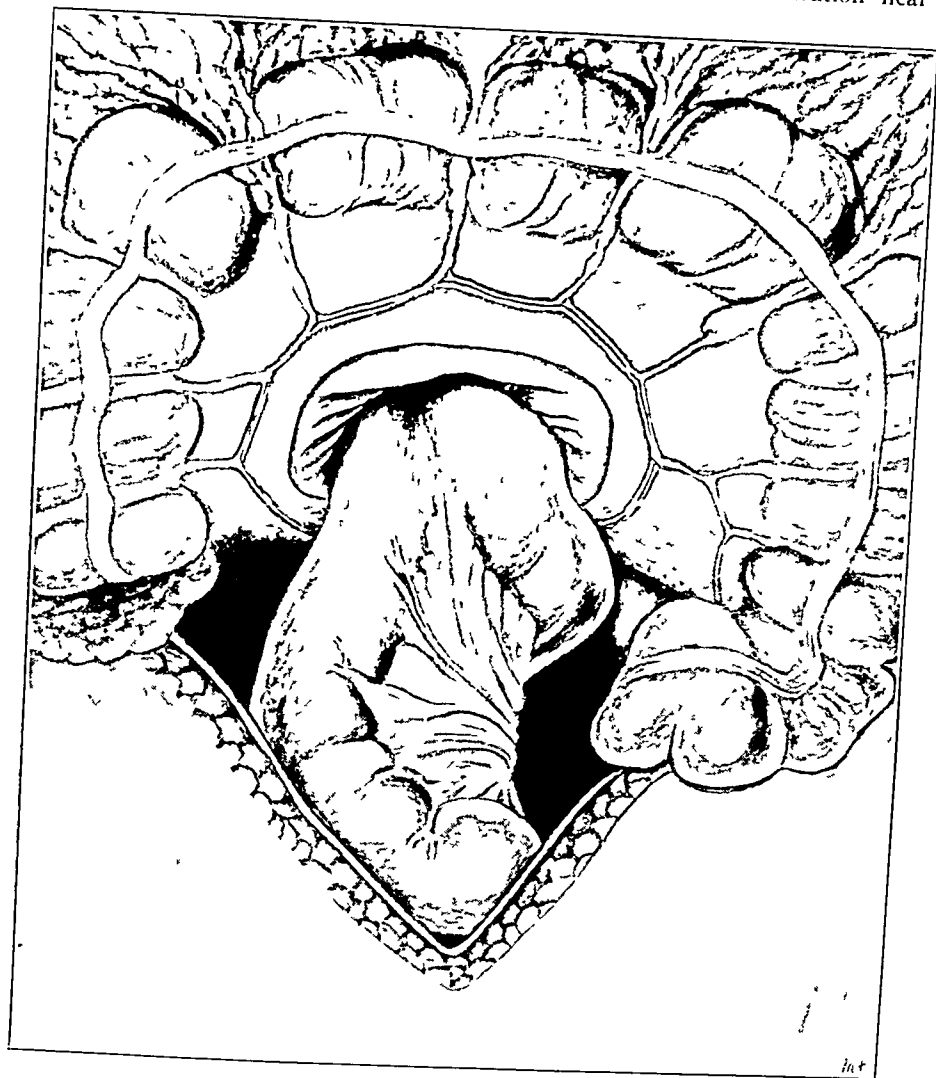


Fig 1—Gastrojejunostomy invaginated into stomach, obstructing adhesions had been removed

pylorus, 2 cm in diameter, on the anterior duodenal wall. A posterior gastro-enterostomy was considered advisable. The cecum was found to be undescended and was held high up under the liver. The appendix contained several hard concretions. The gallbladder appeared normal. An appendectomy was done and a routine posterior gastro-enterostomy performed. The patient was returned from the operating room in good condition. Seven hundred cubic centimeters of

physiologic solution of sodium chloride was given by hypodermoclysis, and 2,000 cc. by proctoclysis.

Progress.—Nothing abnormal was noted on the day of operation or on the second postoperative day. On the third day, there was a burning sensation in the epigastrium. The patient complained of considerable cramplike pain in the right lower quadrant, which was relieved somewhat by a colon tube and enema. On September 9, the administration of liquid diet was begun. The pain in the right

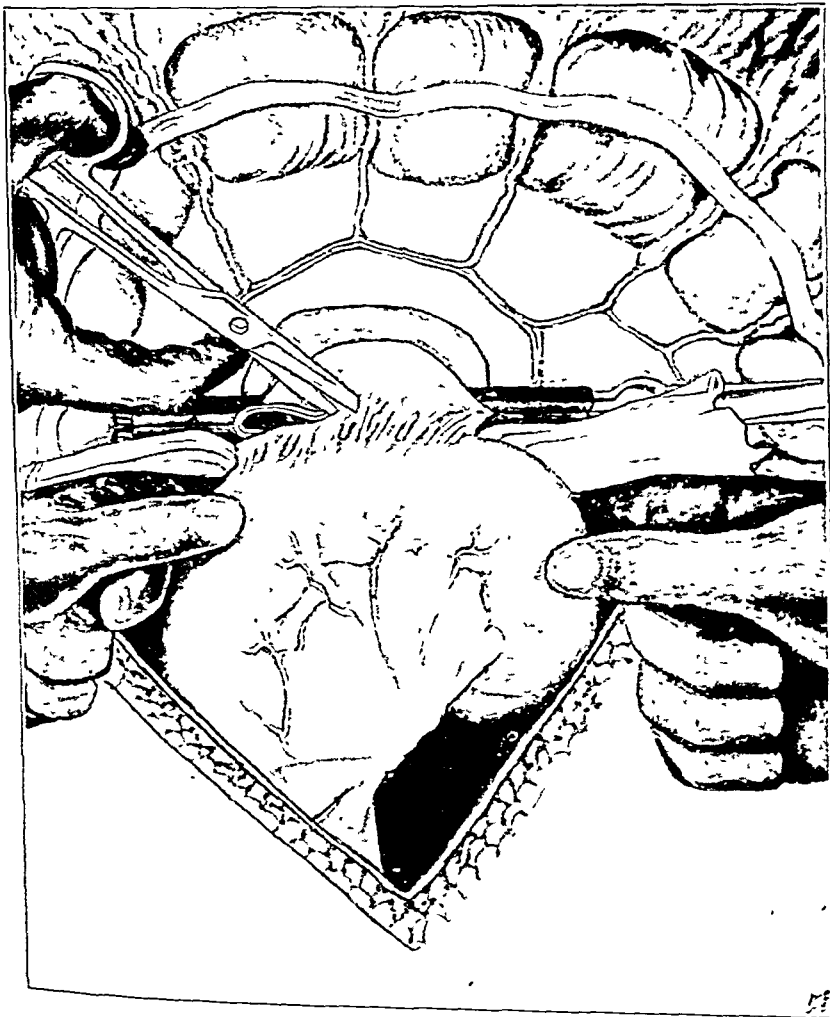


Fig 2—This and the following illustrations show steps in degastro-antrostomy. Invagination is reduced. The gastrojejunostomy is released by sectioning of the stomach, leaving a narrow cuff of the stomach attached to the jejunum.

lower quadrant continued, and the patient complained of thirst. Gastric lavage and enemas gave little relief. On September 10 and 11, nothing noteworthy was observed. On September 12, pain in the right side became severe and was followed by nausea and vomiting. By gastric lavage only a small amount of greenish

mucus was washed out. Thirst was becoming marked. The following day, pain and epigastric burning persisted; lavage was still being used, but little relief was obtained. Proctoclysis, 1,500 cc. of physiologic solution of sodium chloride was instituted. On the afternoon of the eighth day burning in the epigastrium and pain in the right lower quadrant became more severe and rhythmical hiccups developed, occurring from every five to ten seconds. Hoffman's anodyne, atropine, camphor, amyl nitrite and morphine were all tried without avail. Gastric lavage (5 per

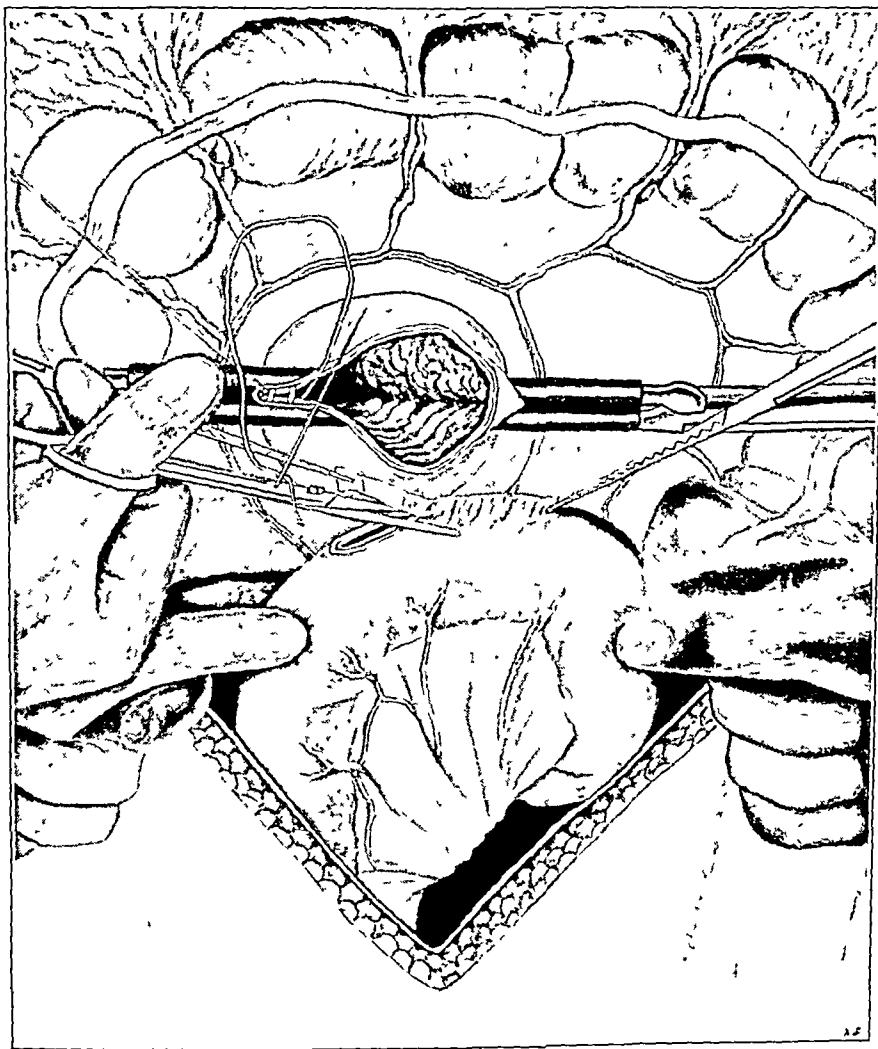


Fig. 3—The upper part of the picture illustrates the suturing of the mucosa of the stomach; the lower part, the removal of the cuff of stomach from the jejunum

cent soda) gave no relief. After thirty-six hours of singultus, the patient fell asleep. An enema given later returned slightly colored, with a small amount of hard, formed feces. No flatus was passed. The cramps recurred. Proctoclysis, 500 cc. of 10 per cent dextrose, was given together with 700 cc. of physiologic solution of sodium chloride by hypodermoclysis. A Levine nasal tube was passed,

and magnesium sulphate injected through the tube produced no results. An enema returned slightly colored.

The patient was almost too weak to talk above a whisper. On the tenth postoperative day, 750 cc. of matched citrated blood was given intravenously, together with 250 cc. of physiologic solution of sodium chloride. On the eleventh day, there was considerable twitching. He talked incoherently. Fluids given by mouth were not retained, so that 1,250 cc. of physiologic solution of sodium chloride was given intravenously. On the twelfth day, the Levine tube was again passed, and 150 cc. of a greenish fluid was aspirated. An enema returned clear. Through the Levine tube, barium meal was injected into the stomach. Careful observation with the fluoroscope for from fifteen to twenty minutes failed to



Fig. 4.—The upper part of the picture illustrates the mucosa of the stomach sutured; suturing muscularis and peritoneum. The lower part shows the suturing of the mucosa of the jejunum.

show any of the barium leaving the stomach. Another 750 cc. of matched citrated blood was given in the afternoon of the twelfth day, and was followed by some heat and itching.

Second Operation.—At 4:30 p. m. on the afternoon of the twelfth day, a second operation was performed. The old incision easily separated and spread open with little evidence of repair. A mass of dense adhesions was found in the area of the operative field. There was a herniation of the jejunostomy anastomosis into the stomach which caused complete obstruction of the duodenum and a few inches of the jejunum below the ligament of Treitz, and closed the gastro-

jejunostomy opening by compression. All of the tissues were densely adherent. The hernia was released and the anastomosis uncoupled. The stomach and jejunum were rapidly closed with double rows of chromic catgut, and the abdomen was closed with through and through silkworm gut sutures. During the operation, the pulse rate had jumped to 164 and the blood pressure dropped to 88 systolic; the diastolic pressure could not be determined. My much interested colleagues and assistants were so exercised, thinking the patient would die on the table, that after the stomach was closed I was urged to put a tube in the jejunum and get the patient to bed. Fortunately, I did not follow this advice. During the operation, 200 cc. of physiologic solution of sodium chloride with



Fig 5—The upper part of the picture shows the burying of the suture line in the stomach by the Cushing right-angle continuous stitch; the lower part, the suturing of the muscularis and peritoneum of the jejunum.

10 minims (0.6 cc) of epinephrine was given intravenously. The patient was returned from the operating room in an extreme state of shock; the body was cold and clammy, and the lips were cyanotic. The pulse could not be felt. Respiration had ceased. The foot of the bed was elevated, and a suction machine was used to remove mucus from the pharynx. A towel clip was put through the tongue to hold it forward and to aid in artificial respiration. Epinephrine, 10 minims, was given intravenously. The entire body was rubbed vigorously. Physiologic solution of sodium chloride with 20 minims (1.25 cc.) of epinephrine was given slowly by hypodermoclysis. After thirty minutes of artificial respiration, the apex beat could be guessed at 165 with the stethoscope. The respirations were

very shallow, but became more regular and full. Oxygen was administered; proctoclysis, with physiologic solution of sodium chloride, was begun. The patient was restless throughout the night. Just before operation a subnormal temperature had jumped to 103 F., the pulse rate to 164 and the respirations to 35. On the second day following, the temperature had dropped to 99.6 F., the pulse rate to 100, and the respirations to 20.

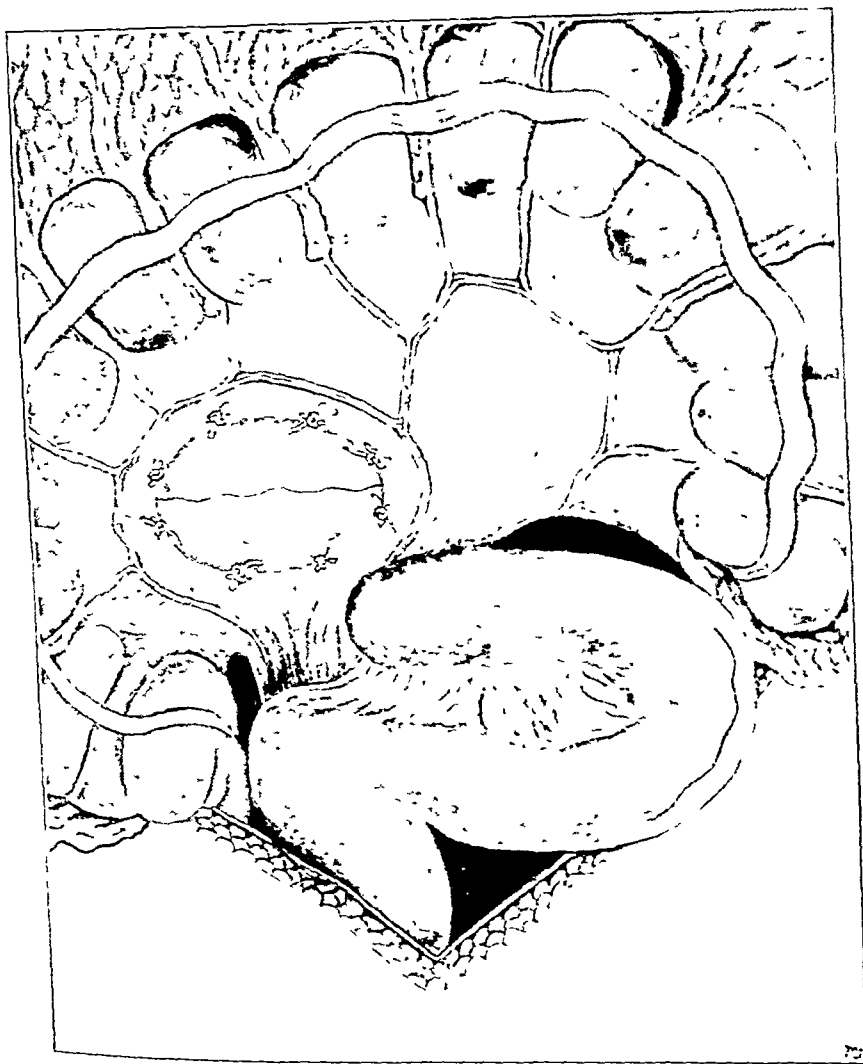


Fig 6.—The stomach is fastened to the mesocolon by interrupted stitches. The wounds in the stomach and jejunum are closed.

Progress.—On September 19, 300 cc. of matched citrated blood was given intravenously, with 250 cc. of physiologic solution of sodium chloride about twenty-four hours after operation. Because of cramping and some nausea, gastric lavage with 2 per cent soda was given: this brought back some clear, dark-colored fluid. Abdominal pains were severe and were best controlled by heroin, which was the only narcotic to which the patient was reasonably susceptible. On September 20,

nausea persisted, but it was not so troublesome as before. There was a severe stomatitis, the result of dehydration. Air hunger was marked. One thousand two hundred cubic centimeters of physiologic solution of sodium chloride with 10 per cent dextrose was administered intravenously. On September 21, the cramps decreased, and the patient began to tolerate some fluids. Epigastric burning was relieved by sodium bicarbonate. On September 25, after ninety-six hours, some soft food was added to the liquids. On the eighth postoperative day, difficulty in swallowing was noted. There was pain underneath the sternum, radiating to the back. It was necessary to discontinue food and liquids for twenty-four hours and to limit the diet for the next three or four days in order to relax a probable cardiospasm. On October 10, the diet was gradually increased, and on the twelfth day the abdominal sutures were removed. Activities were renewed by degrees, and the patient was dismissed from the hospital in good condition on the nineteenth day following the second operation.

COMMENT

The delay in doing the second operation was due to two factors: 1. The patient objected to having anything done, being convinced that he was suffering from a dilated stomach. 2. There were too many physicians interested in the case, and no one was in command.

Since dismissal, or for the last one and a half years, the patient has remained on a soft, acid-free and roughage-free diet, and has not had many symptoms. The weight has returned to normal, and he has carried on his duties, feeling better than before the illness began. He is an active, hard-working man with a healthy appearance. X-ray pictures have demonstrated the stomach and duodenum functioning normally.

From the standpoint of animal experimentation, this man's life was saved from the intoxication of the duodenal block by the administration of large quantities of sodium chloride before and after the release of the obstruction. The symptoms exhibited in this case just before the second operation were not those commonly observed in cases of much lower intestinal obstruction when seen late. They resembled more those seen in infants with congenital pyloric stenosis—the neglected case. I once operated on one of these infants in the stage of convulsions—in fact, it had a convulsion while I was operating, and marvelously, the child lived.

Occasionally, it is necessary to release a gastrojejunostomy. I have employed a technic which when the urgency of the procedure admits is carried out as indicated in figures 1 to 6. Thalheimer⁶ employed a somewhat similar method. It is different in that the closures in the stomach and jejunum are made at right angles to the long axes of the stomach and jejunum; the method of suturing is also different.

6. Thalheimer, M.: *J. de chir.* 30:385 (Oct.) 1927.

PERICARDOTOMY FOR PYOPERICARDIUM *

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When one considers the modern surgical optimism regarding the treatment for pyoperitoneum and pyothorax, the reluctance which has characterized surgical drainage of purulent exudate from the pericardial sac seems difficult to appreciate. In a masterly treatise on this subject, Winslow and Shipley¹ were able to collect only 118 recorded cases from the world's literature dealing with this subject.

Drainage of exudate contained in the pericardial sac was probably first suggested by Riolanus,² in 1648. It was not until 1855, however, that drainage of the pericardial sac through an opening in the sternum was first practiced by the Frenchman, Malle.³ Larrey,⁴ in 1829, first successfully employed the xiphocostal route. It remained for Hilsmann, in 1844, to cure a patient of pyopericardium by the performance of pericardotomy. Little attention was paid to the procedure until 1879, when the classic report of Rosenstein focused attention on the possibilities of the operation. More recently the successes of Winslow and Shipley and Peterson⁵ should serve to popularize this relatively simple procedure; in the opinion of the former writers, operative treatment should yield about 70 per cent of cures.

The purposes of this paper are to discuss briefly the etiologic factors responsible for the disease and its diagnostic characteristics, to describe a recent experience and to outline a simple operative procedure.

In all probability, suppurative pericarditis never primarily arises in the pericardium. In most instances it represents an extension of some infectious process of the lung and pleura. Lobar (pneumococcus) pneumonia invariably extends to the pleura, producing an inevitable fibrino-purulent pleuritis. In many instances, pyothorax results and may involve the pericardium by contiguity. In many cases, the disease has followed perforating knife or bullet wounds with direct implantation

* Submitted for publication, April 4, 1929.

* From the Dayton Clinic.

1. Winslow, N., and Shipley, A. M.: Pericardotomy for Pyopericardium, Arch. Surg. 15:317 (Sept.) 1927.

2. Riolanus, quoted by Hindenlang: Deutsches Arch. f. klin. Med. 24:452, 1879.

3. Malle: Traité d'anatomie chirurgicale et de médecine opérative, Paris, 1855, p. 888.

4. Larrey: Clin. Chir. 2:303, 1829-1836.

5. Peterson, E. W.: Suppurative Pericarditis: Report of Three Cases, Arch. Surg. 16:366 (Jan.) 1928.

of the infective agent. In other instances, the pyopericardium has been attributed to a local manifestation of a septicopyemia, such as that associated with osteomyelitis.

The failure to make a proper diagnosis of pyopericardium is so often revealed at the autopsy table that a brief recitation of the essential diagnostic criteria seems justified. The first requirement is the recognition of those diseases in which pyopericardium is a secondary manifestation.



FIG. 1.—Roentgenogram of chest showing greatly enlarged heart shadow and left pneumothorax.

If this is accompanied by a careful consideration of the history and physical examination, together with roentgenographic studies and diagnostic aspiration, the diagnosis should present no great difficulties. The most common physical signs are enlargement of the area of precordial dullness, frequently with shifting of the upper limit of dullness on changing the position, rapid pulse and respiration, muffled heart sounds, friction rub in the early stages and dull tympany over the infrascapular area. The difficulties encountered in distinguishing pyopericardium from car-

diac dilatation are indicated by the frequent performance of paracentesis cordis when paracentesis pericardii was being attempted. In simple dilatation the heart sounds are clear and sharp, whereas in pericardial effusions the sounds are distant and muffled.

REPORT OF CASE

B. L., a youth, aged 17, was first seen by Dr. P. A. Kemper, Germantown, Ohio, on April 12, 1928, when he complained of severe pain in the lower left side

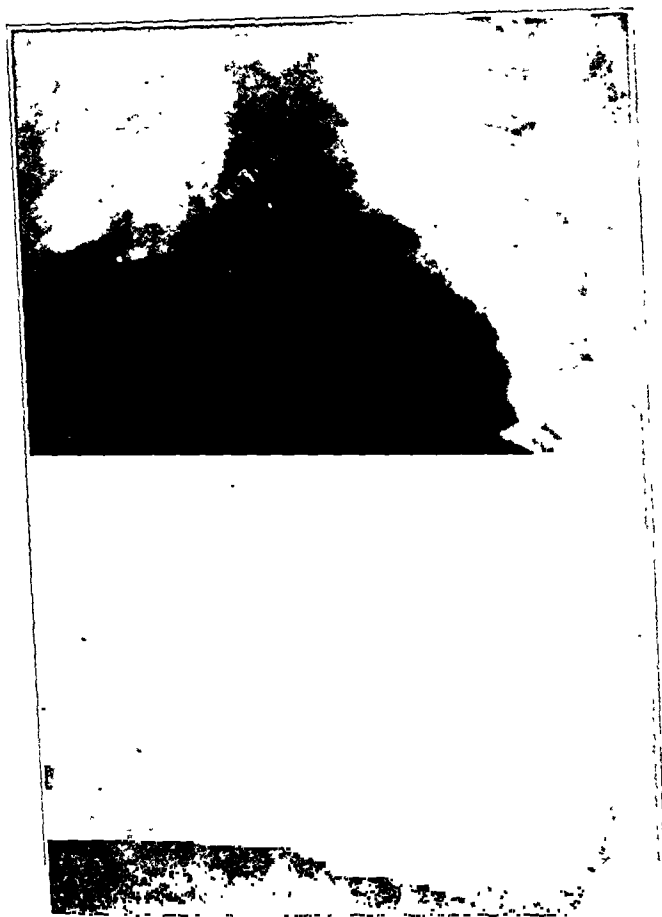


FIG. 2.—Roentgenogram taken after aspiration of 925 cc. of turbid semipurulent fluid from pericardial sac, showing little decrease in size of heart shadow.

of the chest. He had a nonproductive cough, temperature of 102 F., pulse rate of 100 and increased respiratory rate. Physical examination revealed dulness over the lower half of the left side of the thorax. A diagnosis of lobar pneumonia was made. During the next five days, the symptoms and signs were aggravated. Ten days after the onset of illness, flatness was found on percussion, and drainage by the closed method yielded 1 liter of turbid straw-colored fluid during the first twelve hours. From April 22 until May 1, a moderate amount of exudate escaped, at the end of which time the patient experienced repeated chills and

sweats, dyspnea and cyanosis. On May 3, he complained of pain over the area of the liver. Dr. Kemper found considerable enlargement of the liver. At this time the heart sounds became more distant, the area of cardiac dulness became larger and the patient became orthopneic. The pain shifted to the interscapular region and increased as the area of cardiac dulness became larger.

On May 5, 1928, the patient was referred to me, with the diagnosis of left-sided lobar pneumonia, with empyema and purulent pericarditis. On admission to the Miami Valley Hospital, respirations were labored, even when he was in a sitting position; cyanosis was marked; the dulness around the liver extended

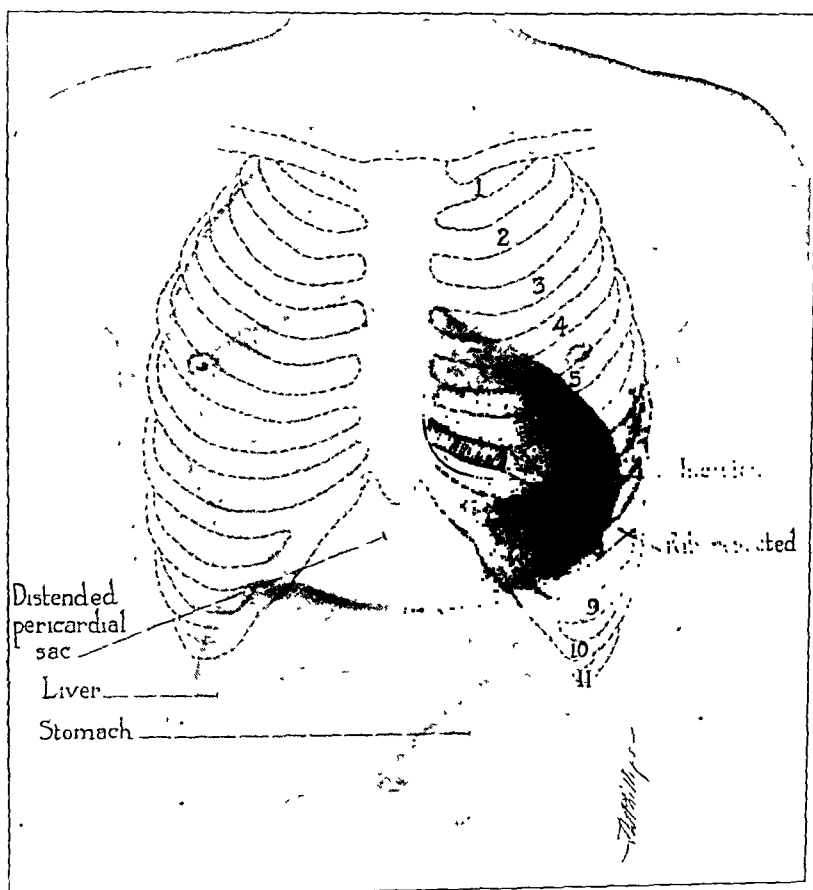


FIG. 3.—Drawing showing location of curvilinear incision along the left border of the sternum, beginning at the fifth left sternochondral junction and extending lateralward just below the inferior border of the sixth rib.

below the umbilicus; the superficial thoracic veins were greatly dilated; the heart sounds were distant and muffled; the area of cardiac dulness was greatly widened, and the legs were edematous. The temperature was 101 F., the pulse rate 120 and respirations 35. Fluoroscopic examination and stereoscopic films of the chest (fig. 1) showed a heart shadow which occupied fully three fourths of the thoracic cavity, together with left pneumothorax.

On May 7, 925 cc. of turbid, semipurulent fluid was aspirated from the pericardial sac. This gave the patient temporary relief from his respiratory embar-

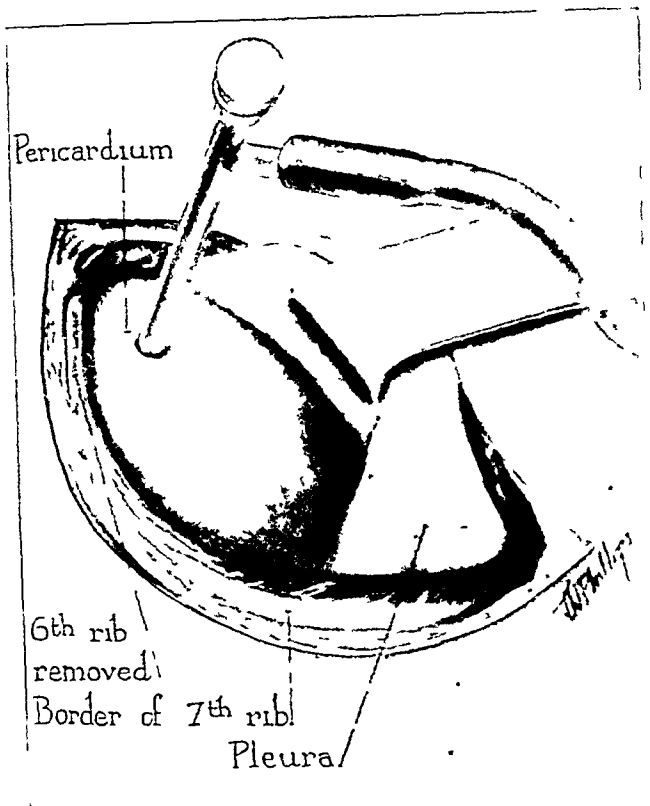


FIG 4—Drawing showing method of introduction of gallbladder trochar into pericardial sac

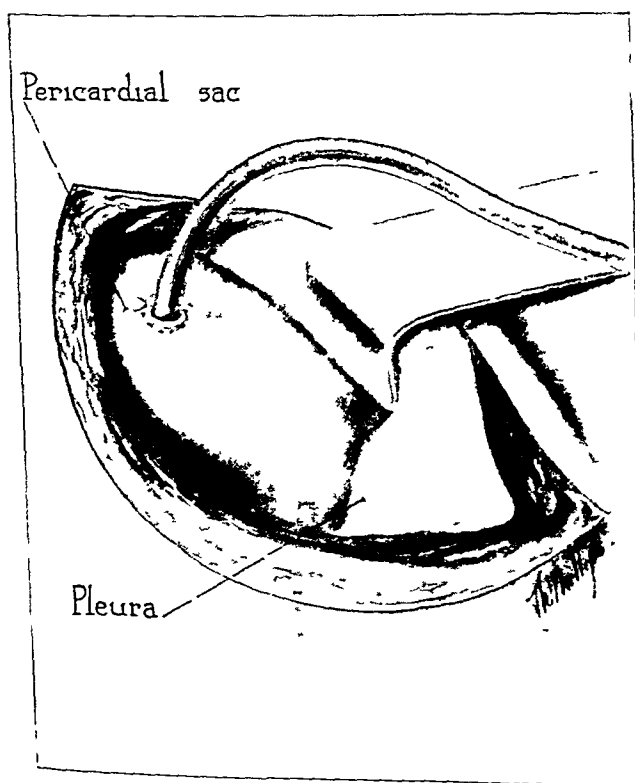


FIG 5—Drawing showing position of catheter fixed with purse-string suture

rassment, but did not appreciably decrease the area of dulness around the heart (fig. 2). Pneumococci were recovered from the aspirated exudate. During the next twenty-four hours, the patient became obviously worse, and on May 9, pericardotomy was done under local anesthesia.

A curvilinear incision was made along the left border of the sternum, beginning at the fifth left sternochondral junction and extending lateralward just below the inferior border of the sixth rib to a point 2 cm. to the left of the costochondral junction (fig. 3). The flap was dissected upward from the underlying rib, exposing the costal cartilage of the sixth rib. The costal cartilage was removed.

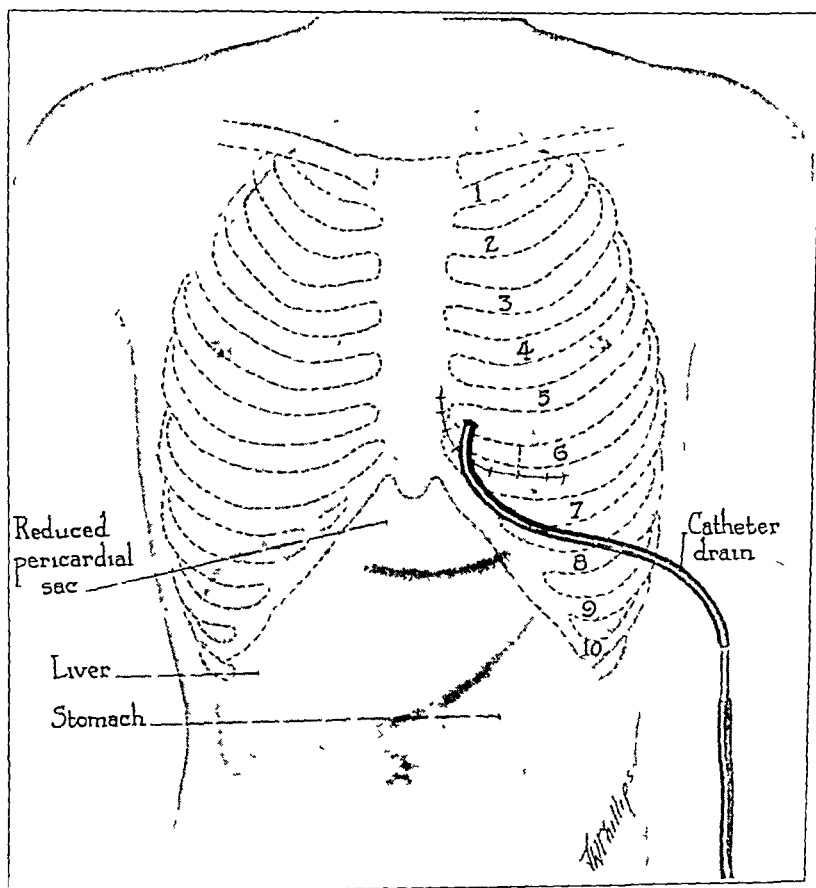


FIG. 6.—Drawing showing point of exit of catheter through stabwound in fifth intercostal space 1 inch above incision. The catheter is connected with a tube leading to a drainage bottle.

The pleura and lung were drawn lateralward by means of a broad retractor with a short hook. An aspirating needle attached to a Luer syringe was then introduced into the pericardial sac to determine the depth and location of the exudate. This was followed by the introduction of a gallbladder trochar into the sac (fig. 4). Approximately 600 cc. of thick purulent fluid escaped by gravity through the trochar and attached tube. A large Luer syringe was then attached to the free end of the tube and about 200 cc. of purulent fluid were withdrawn by suction. A purse-string suture was placed around the trochar, after which it was with-

drawn from the sac and a male catheter of similar caliber introduced and fixed with the purse-string suture (fig. 5).

The pericardial sac was then irrigated with 1 liter of physiologic solution of sodium chloride, at the end of which time the fluid returned clear. During the irrigation many large flakes of fibrin were washed out. The catheter was then drawn through a stab wound 1 inch (2.5 cm.) above the incision, near the sternum, and the wound was closed with interrupted sutures. The drainage tube was then connected with a tube leading into a large bottle containing antiseptic fluid (fig. 6).

The patient experienced immediate relief from the dyspnea and cyanosis, and the dependent edema rapidly diminished. The liver decreased in size and the



FIG. 7.—Heart showing typical fibrinopurulent pericarditis ("cor villosum" or "shaggy heart").

cardiac shadow returned to approximately normal. The lumen of the catheter was kept open by daily injections of sterile saline solution.

During the four days following the operation, the patient showed marked improvement. On the fifth day, however, he showed signs of overwhelming sepsis, and he died on May 16, one week after operation.

Post-mortem examination revealed: left empyema (pneumococcus type); complete atelectasis and unresolved lobar pneumonia of the left lung; fibrinopurulent pericarditis ("cor villosum" or "shaggy heart") (fig. 7); organizing right-sided adhesive pleuritis; marked cloudy swelling, fatty degenerative infiltration and chronic passive congestion of liver, kidneys and myocardium; ascites of mild degree, and edema of the legs.

COMMENT

The immediate response to the simple operation was striking and gratifying. In view of the fact that the exudate which collects in the relatively small pericardial sac can find no physiologic outlet, it seems logical to contend that the early institution of surgical drainage offers to the patient his greatest hope. Two factors are in operation which constitute a serious handicap to the heart's work: first, the degenerative effects on the myocardium produced by the local inflammatory process; and second, the mechanical handicap produced by the rapidly increasing imprisoned exudate in the sac. Pericardotomy is a simple operation, presenting little or no risk, and is capable of saving life. The foregoing operative procedure is presented with the hope that it will stimulate others to give it a fair trial.

GANGLIONEUROMA OF MEDIASTINUM REQUIRING SURGICAL INTERVENTION FOR RELIEF OF OBSTRUCTIVE SYMPTOMS*

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AND

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Patients on whom it is possible to use only palliative surgical procedures are, unfortunately, often seen. Occasionally, the pathologic condition found gives rise to considerable discussion because of its relative infrequency.

Mediastinal tumors requiring surgical intervention because of symptoms of tracheal obstruction are rare. Of these, tumors arising from the sympathetic nervous system are perhaps the most rare. Because of its rarity and interest, we wish to report a case of ganglioneuroma apparently arising from the thoracic or the cervical segment of the sympathetic system.

REPORT OF A CASE

History.—A. B., a boy, aged 4 years, was admitted to St. Mary's Hospital on Nov. 20, 1925, with the complaint of difficulty in breathing and of swelling in the right side of the neck. The maternal grandfather was said to have died of cancer of the stomach and the paternal grandmother of cancer of the liver. A paternal uncle had died suddenly at the age of 6 months from an unknown cause. The boy was born on Oct. 22, 1921, delivery being normal. The mother did well and the child developed normally. No abnormality was noted in the other children in the family and there had been no serious diseases. The patient had had no headaches, pain in the chest, croup, gastro-intestinal disturbances or genito-urinary disease. Movements of the bowels were regular. He had a light attack of influenza in January, 1924, and contracted scarlet fever on March 1, the same year.

Three weeks after the onset of scarlet fever, or on March 22, a swelling was noted in the right anterior cervical triangle. The parents were assured that the condition was probably secondary to scarlet fever. The swelling persisted for nineteen months, but no symptoms developed until the latter part of October, 1925, when the patient had a severe cold, persistent cough, increasing hoarseness and pressure symptoms.

Examination.—The patient was a moderately nourished boy in considerable respiratory distress, as evidenced by cyanosis, stertor and voluntary respiratory efforts. There was a fulness in the right anterior triangle of the neck similar to that of a tuberculous adenitis. The left side of the neck was apparently normal. The right pupil was larger than the left, and the pupillary reflex was diminished. The tonsils were of the cryptic type, touching in the midline. On palpation of

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* Read before the Western Surgical Association, Dec. 15, 1928.

the right side of the neck, there seemed to be two masses, each composed of lobules, rather firm, attached to the deep structures but not to the overlying skin. They were not tender. One mass extended from beneath the sternomastoid muscle toward the midline, while the other extended downward and was lost beneath the clavicle. Examination of the chest was unsatisfactory, owing to the respiratory noise.

Laboratory Observations.—On November 20, the urine was normal. The blood showed: red blood cells, 3,530,000; hemoglobin, 70 per cent (Dare); color index, 1; white blood cells, 5,500; polymorphonuclears, 65 per cent; small lymphocytes, 27 per cent, and transitionals, 8 per cent. The blood pressure was not taken. On Jan. 8, 1926, the blood showed: red blood cells, 2,500,000; hemoglobin, 52 per cent (Dare); white blood cells, 21,300; polymorphonuclears, 84 per cent; small lymphocytes, 9 per cent; transitionals, 5 per cent; polymorphonuclear eosinophils, 1 per cent, and polymorphonuclear basophils, 1 per cent.



Fig. 1.—Roentgenogram taken at the time of admission, showing a shadow in the right apex.

On Nov. 21, 1925, the roentgen report was: "There is a mass in the upper thorax which extends above the clavicle on the right side. The right border is well marked extending outward to the juncture of the middle and distal thirds of the clavicle and passing downward to the level of the fifth thoracic vertebra and rounding off toward the midline to be lost in the shadow of the spine. On the left, the border is not well marked, but the trachea is seen displaced somewhat to the left. This mass is smooth in outline and of uniform density. No changes of the bone are noted.

"Conclusion: This may be an abnormal thyroid; a thymus, or an 'hygroma.'"

Operation.—On the basis that the condition might possibly be an abnormal thymus, the patient was given four roentgen treatments, three over the upper thorax and one deep irradiation of the chest, but without appreciable benefit. On December 10, with the patient under an ether rausch, the tonsils and adenoids were removed in the hope that part of the respiratory obstruction might be relieved and as a preparatory step to a possible later operation on the neck. Section of the tissue

of the tonsil showed lymphoid hyperplasia and no other pathologic changes. On December 16, a second roentgen examination was made, concerning which the following report was made:

"Screen Examination: The cardiac shadow appears normal. There is a mass in the mediastinum extending down to the second interspace. It extends to the right displacing the right apex. Plate Examination: The cardiac shadow is normal; the bases are clear; there is an area of increased density involving the upper mediastinum from the level of the sixth dorsal vertebra upward. On the right it forms a curved line outward and upward obliterating the apex of the right lung and involving the neck above the clavicle. When compared with the previous x-ray there is no evidence of increase in size.

"Impression: Probable lymphosarcoma."

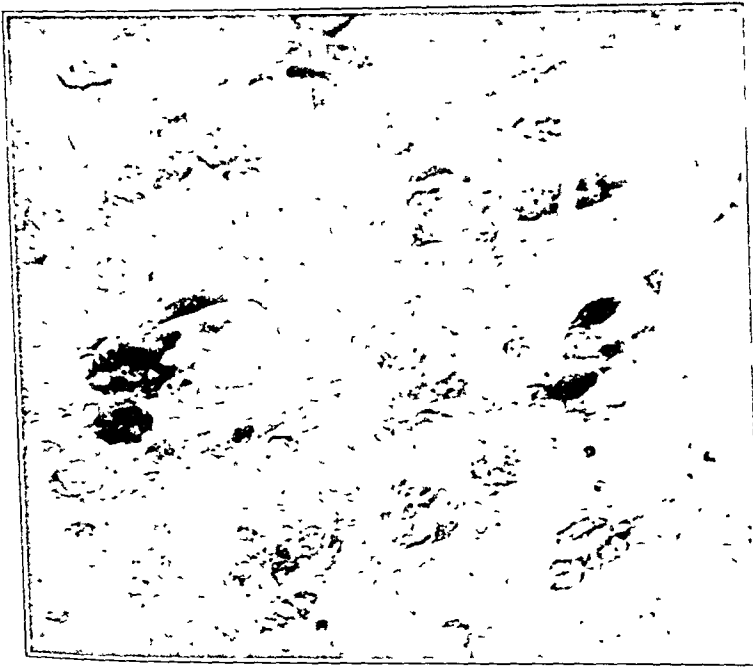


Fig. 2—Ganglion cells distributed throughout section, many showing nuclei and nucleoli. Homogeneous supporting tissue. Note the tendency to grouping of the cells. Hematoxylin and eosin; $\times 157$.

Course.—The patient was then temporarily discharged to recover from the tonsillectomy, and was readmitted on Jan. 6, 1926, at which time a roentgen examination showed a definite displacement of the trachea to the left at the level of the lower cervical and upper thoracic vertebrae. The patient's condition was pitiful—a typical picture of tracheal obstruction in an extreme form.

On January 9, an operation was done to relieve the tracheal obstruction, the various preoperative diagnoses recorded at that time being lymphosarcoma, lymphadenoma and thymoma. The gravity of the condition had been and was again fully explained to the parents, who were given to understand that we hoped for little more than temporary relief, and that a complete cure was out of the question.

A "T" shaped incision was made, one portion being parallel to the upper border of the clavicle and the other extending upward along the posterior margin of the sternomastoid muscle. A large mass of nodules was found deep in the neck,

intimately jointed with the right lobe of the thyroid and displacing the trachea to the left. This mass was removed and dissection carried downward underneath the clavicle, new growth being removed from about the common carotid artery and from above and beneath the subclavian vessels, and a mass of the growth was palpated in the mediastinum. It was impossible to determine the size or the extent of the growth. The incision was closed after a small roll rubber drain was placed at the lower point. Convalescence was rather slow and stormy but satisfactory in that the patient was completely relieved from dyspnea, which did not recur until a short time before death nearly eighteen months later.

On January 27, roentgen examination showed that the mass in the upper part of the right side of the chest was somewhat larger than on previous examinations. At the base of the right lung there was an area of increased density involving the lower third of the right lung field; this was more dense in the mesial half. There was a well marked, smooth, upper border suggesting either pneumonia, or a presence of fluid, but it may have been a metastatic growth.

The patient's temperature record showed marked variations. At the time of the first admission the temperature was normal and continued so, save for an occasional slight rise after roentgen therapy, until on December 4 when, without apparent cause, it began to rise, reaching 104 F. within twenty-four hours and dropping back to normal within forty-eight hours. Again after the tonsillectomy on December 10, there was a second similar febrile period, which subsided more slowly. At the time of the second admission, the temperature varied between 97.8 and 100.4 F. until after the operation on the neck, when it rose rapidly to 105 F. and was accompanied by a fine, general scarlatinal rash which was of not more than twenty-four hours' duration and was not followed by desquamation. The temperature, however, remained irregularly elevated for several days, subsiding gradually to normal for the first time on January 26, fifteen days after the operation.

After being discharged from the hospital, the patient was taken home, and letters from his parents reported him as playing actively and normally with his companions and being entirely relieved from his discomfort.

On May 16, 1926, he was again seen and appeared the picture of health. There was no palpable recurrence at the site of operation but percussion showed diminished resonance in the right apex. The report of the roentgen examination at that time was as follows:

"Plate examination of the chest shows a normal cardiac shadow. The diaphragm is normal in outline and the bases are clear. There is a definite shadow in the upper mediastinum which blends with the cardiac shadow. This increased density extends upward and to the right with a clearcut border and involves the right apex. There is also apparently an increased density in the neck on the right side. On the left the border of the heart blends with this mediastinal shadow which extends up to the level of the clavicle about 2 cm., to the left of the spine. When compared with the plate taken on Jan. 27, 1926, the shadow in the mediastinum shows no change. The increased density in the neck above the right clavicle is definitely less than it was at that time and the cloudiness at the right base has all disappeared.

"Conclusion: Tumor of the mediastinum."

The observations and the prognosis were again carefully explained to the parents, and permission, both verbal and written, was obtained for a necropsy when death occurred.

In June, 1926, the parents reported that they were putting the child in the care of a physician of another town who "treated by colored light." On April 2,

1927, the child was seen by Dr. Hagin and Dr. Gregory of Miller, S. D., who took a roentgenogram and confirmed our statement that the outlook was extremely grave, although stating that at that time the child's general condition was not acutely serious. They found a temperature of 100.4 F. and 13,000 leukocytes, and a blood smear showed some degeneration of the red corpuscles but no predominance of lymphocytes.

In May, 1927, the patient's condition began to decline, and on May 19 he was seen by Dr. C. E. Price of Orient, S. D. At that time the parents assured Dr. Price of permission for a necropsy. Shortly thereafter the patient developed a general edema, marked ascites and a recurrence of dyspnea. Death occurred at 6 p. m. on June 3, 1927. The parents absolutely refused a postmortem examination, which is greatly to be regretted, for study of the mass in the mediastinum and that in the area of the lung would have been most interesting and doubtless exceedingly instructive.

Pathologic Data.—Grossly, the material removed was of two kinds, one cellular and friable containing scattered yellowish pinpoint areas and the other grayish white, rather uniformly firm but elastic, each unit or nodule apparently having a thin covering or capsule. The former proved to be thyroid and the latter, neoplasm. On section, the tumor appeared to be made of a fine, closely interlacing structure which was grayish white and firm. A fibrous capsule was present and varied from 1 to 2 mm. in thickness.

The tumor was fixed in a diluted solution of formaldehyde, U. S. P. (1:10). It was embedded in paraffin from which sections were cut and stained with hematoxylin and eosin, van Gieson's stain, Orlandi's modification of Bielschowsky's silver method, thionin, Mallory's phosphotungstic acid and Weigert's myelin-sheath stains.

On microscopic examination, the tumor was fairly dense and consisted mainly of an interlacing fibrous framework supporting some nonmedullated nerve fibers. Ganglion cells were rather evenly distributed throughout the tumor mass. They usually occurred singly, though in places they were seen in groups (fig. 2). Most of these cells were mature, but they varied in size considerably. Some of them were multinucleated (fig. 3), each nucleus having a distinct nucleolus. In some of the cells, the nucleus appeared to be in a process of division while in others the nuclei were widely separated. The cytoplasm apparently was unaffected by the nuclear division. Nissl's granules were distributed throughout the cytoplasm (fig. 4), with a tendency to greater density about the periphery. Many of the cells were surrounded by a definite nucleated capsule. In sections stained by Orlandi's silver impregnation method, definite dendritic processes could be seen to come from the cells (figs. 5 and 6). These processes forked at varying distances from the cell. Many of the cells had undergone cystic degenerative changes (fig. 3).

In no section examined were there "rosetts" or undifferentiated cells suggesting neuroblasts which are occasionally associated with ganglioneuromas.

ORIGIN OF GANGLIONEUROMA

Perhaps the outstanding paper in English on the subject of neuroblastoma and ganglioneuroma is that by Wahl,¹ who gave a concise but thorough review of the literature to 1914. We have drawn freely

¹ Wahl, H. R.: Neuroblastoma. With a Study of a Case Illustrating the Three Types that Arise from the Sympathetic System, *J. M. Research* 30:205, 1914.



Fig. 3.—Multinucleated ganglion cells with Nissl's granules. Note the characteristic nuclei and nucleoli. Tendency for cystic degeneration of these cells (a). Thionin; $\times 450$.

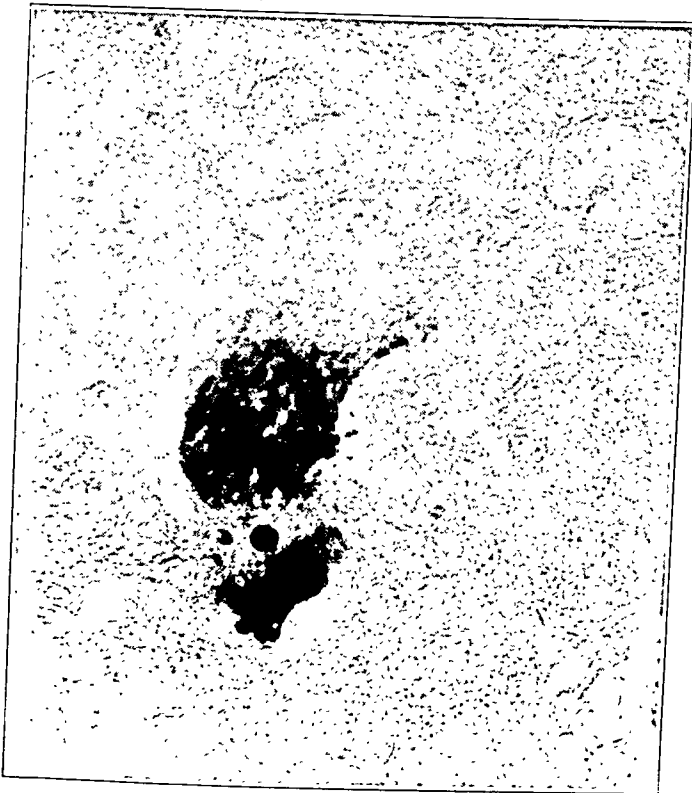


Fig. 4.—Ganglion cell with single nucleus and a distinct nucleolus. Note the Nissl granules. Thionin; $\times 1,000$.



Fig 5—Ganglion cell with multiple dendrites, one of which divides some distance from the cell. Orlandi, $\times 450$



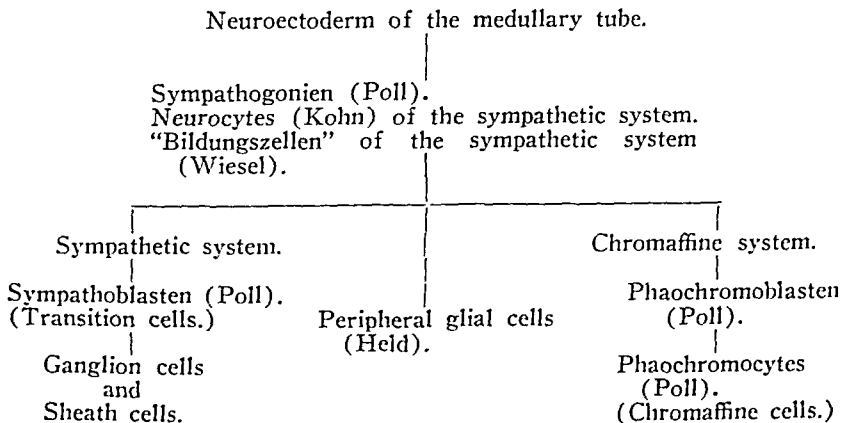
Fig 6—Ganglion cell showing a dendritic process which divides shortly after leaving the cell Orlandi; $\times 450$.

on this paper for information in making a study of our case. He pointed out, in the light of Kohn's work on the development of the sympathetic system, that "The embryonic sympathetic cells are not migrating pre-formed ganglion cells but are simple neurocytes formed in situ that have, locally, a different power of differentiation from elsewhere, in that they become differentiated on the one hand to ganglion cells, capsule cells, nerve fibers, and sheath cells and even glial cells, and on the other hand, to the chromaffine cells."

Simply stated, tumors of the sympathetic system arise from a cell rest, a mother cell called the neurocyte which has multipotential characteristics. The type or types of cells which characterize a tumor arising from the sympathetic nervous system depend, therefore, on the degree of differentiation to which the cells composing it have progressed.

CLASSIFICATION

Tumors arising from the sympathetic nervous system are divided into three main groups: (1) the neuroblastoma, (2) the ganglioneuroma and (3) the paraganglioma. The neuroblastoma is composed of undifferentiated cells and is malignant. These cells resemble lymphoid cells and are frequently arranged in rosets. The ganglioneuroma and paraganglioma are composed of highly differentiated cells and are benign. The former consists chiefly of ganglion cells, while the latter consists of cells having great affinity for the chrome salts similar to those of the medulla of the suprarenal gland. Between the undifferentiated cells of the neuroblastoma and the fully differentiated cells of the ganglioneuroma and paraganglioma there are cells in various stages of transition known as transitional cells. The genetic relation of the different nerve elements of which such tumors are composed is clearly expressed in the following scheme taken from Wahl.¹



This genetic relationship makes it easy to understand the varied histologic picture which is frequently encountered in a single tumor.

Two or more nerve elements frequently have been observed in a single case, and in the case presented by Wahl all three types of tumor were present.

A girl, aged $2\frac{1}{2}$ years, was markedly anemic and had had abdominal symptoms for several months, with irregular temperature, abdominal distention and enlargement of the inguinal lymph nodes. On examination, an irregular firm and fixed mass was found in the umbilical region. The postmortem observations as they pertain to this case were: malignant neuroblastoma of the sympathetic system arising in the left suprarenal gland and celiac plexus with metastasis to the liver, lymph glands, kidneys and left suprarenal gland; ganglioneuroma and paraganglioma of the left suprarenal gland.

To indicate the occurrence of two or more types of cells in a tumor, Robertson,² in 1915, suggested a fourth group. In this group, he placed tumors of group 1 in combination with either group 2 or 3, or both. For example, the tumor in Wahl's case would be designated ganglioparaganglioneuroblastoma and would be placed in group 4.

In the same year, Dunn³ reviewed the literature on the subject and grouped the tumors according to the region from which they had arisen. He collected fifty-one cases, the tumors of which had taken their origin in the following regions: four in the cervical segment, five in the thoracic segment, nineteen in the abdominal segment, eleven in the suprarenal gland, two in the subcutaneous tissue, four in the central nervous system and six in the peripheral nerves.

Reports of about sixty-five cases of ganglioneuroma are now recorded in the literature. Of this number, there are six cases which apparently have arisen intrathoracically; there are three cases, including ours, which have involved both the neck and the thorax and there are three cases which have been reported as arising in the neck (tables 1 and 2).

Loretz⁴ is credited with having given the first description of ganglioneuroma and, incidentally, of one of the cases of intrathoracic ganglioneuromas:

A woman, aged 35, was found unconscious and in convulsions. She died the same day, and at autopsy, a smooth subpleural tumor, 7.5 by 4.5 by 4.5 cm., was found in the left thoracic cavity in the region of the second and third thoracic vertebrae. Grossly it was composed of two layers. The outer layer was light and consisted of fibrous tissue, blood vessels and fatty tissue. The central layer was more grayish and softer, resembling a section of the uterus. It consisted mainly of nonmyelinated nerve fibers in which there were rather typical ganglion cells.

2. Robertson, H. E.: Das Ganglioneuroblastom, ein besonderer Typus im System der Neurome. *Virchows Arch. f. path. Anat.* **220**:147, 1915.

3. Dunn, J. S.: Neuroblastoma and Ganglioneuroma of the Suprarenal Body. *J. Path. & Bact.* **19**:456, 1914-1915.

4. Loretz, W.: Ein Fall von gangliösem Neurom (Gangliom). *Virchows Arch. f. path. Anat.* **49**:435, 1870.

The case reported by Martius⁵ closely resembles the one reported by us and is worthy of being recorded here:

A boy, aged 2½ years, had a tumor in the right side of the neck which displaced and compressed the trachea. He was operated on because of dyspnea. At operation, the tumor was found intimately associated with the right lobe of

TABLE 1.—*Intrathoracic Ganglioneuroma*

No.	Author	Year	Sex	Age	Site	Size
1	Loretz, W.: Virchows Arch. f. path. Anat. 49: 435, 1870	1870	F	35	Left thorax; second and third dorsal vertebrae	7 by 4.5 by 4.5 cm
2	Borst, M.: Die Lehre von den Geschwulsten. Munich, J. F. Bergmann, 1902, vol 1, p. 241	1902	?	?	Left subpleural	Child's head
3	Rindfleisch, E.: Quoted by Borst	1902	?	?	Angle of wall of rib and anterior circumference of spine	?
4	Benda, C.: Verhandl. d. deutsch. path. Gesellsch. 7: 266, 1904	1904	?	Child	Right side of neck and thorax	Apple
5	Friedrich, J.: Frankfurt. Ztschr. f. Path. 10: 456, 1912	1912	F	73	Sixth to eighth right thoracic vertebrae	7 by 2.8 cm
6	Martius, K.: Frankfurt. Ztschr. f. Path. 12: 442, 1913	1913	M	2½	Right side of neck and thorax	3.5 by 2 by 0.75 cm.
7	Tschistowitsch, F. J.: Zentralbl. f. Chir. 35: 576, 1908	1908	F	12	Fourth to sixth right thoracic vertebrae	Goose egg
8	Brunner, A.: Arch. f. klin. Chir. 129: 364, 1924	1924	F	19	Second to ninth dorsal vertebrae; left thorax	17 by 12 by 8 cm
9	Riggs and Good	1928	M	4	Mediastinum and right side of neck	Not determinable

TABLE 2.—*Ganglioneuroma Arising in the Neck*

No	Author	Year	Sex	Age	Site	Size
1	Gliniski, S. K.: Deutsche med. Wehnschr. 32: 2044, 1906	1906	?	10	Deep in left side of neck	9 by 6.5 cm
2	Woods, C. S.: Deutsche med. Wehnschr. 32: 2044, 1906	1906	M	32	Right carotid sheath	9 by 8 by 4 cm
3	Freund, P.: Frankfurt. Ztschr. f. Path. 13: 266, 1913	1913	M	5¼	Right side of neck	9 by 6 by 4 cm

the thyroid from which it was thought to arise. The patient died a short time later. At autopsy, two masses of tumor were found. One was nodular and extended from the right side of the thymus downward and medially to the right atrium, and surrounded the superior vena cava and main bronchus. This tumor mass contained undifferentiated and partly differentiated cells and was malignant. To the side and below, and somewhat separated from this mass, was a tumor

⁵ Martius, K.: Maligner Sympathoblastentumor des Halssympathikus teilweise ausdifferenziert zu gutartigem Ganglioneurom, Frankfurt. Ztschr. f. Path. 12: 442, 1913.

occupying the angle formed by the first and second ribs with the spine. It was 3.5 by 2 by 0.75 cm., smooth and firm and resembled a myoma. The tumor was composed of well differentiated ganglion cells and nonmedullated nerve fibers. It was considered benign. It was thought that the two masses of tumor had a common origin in the sympathetic nervous system, and that they differed only in degree of differentiation. As the sympathetic system from the midcervical to the first thoracic was intimately involved in the tumor, it was considered to have arisen in this region.

In 1924, Brunner⁶ reported a case:

A girl, aged 19, for a period of two months previous to coming under his care, had had oppressive pain in the back and left side when lying down. Because of the pain, she could lie down only half an hour at a time. She obtained immediate relief on sitting up. Various diagnoses had been made, the final one being intra-thoracic dermoid cyst. On examination, the patient was found to be of medium size. From the upper border of the scapula down to about the tenth dorsal vertebra there was almost complete dullness, and over which the breath sounds were diminished.

Roentgen and fluoroscopic examination showed a nonpulsile shadow, the size of a child's head, extending from the second to the ninth dorsal vertebra on the left. It was in close relationship to the spine. The anterior mediastinum was clear.

The patient was operated on by Sauerbruch. A paravertebral incision was made, and several ribs were resected over the mass. Exploration revealed a smooth, firm, round tumor slightly adherent to the pleura and markedly adherent around the aorta. The tumor arose from the posterior mediastinum, pushing the lung ahead of it. No attempt was made to remove the tumor at this stage. The cut edges of the pleura, however, were stitched to the tumor mass. At a later date, a second stage operation was done, at which time the tumor was removed with great difficulty. The patient had a stormy convalescence, developing a sterile empyema and finally a necrosis of the left lung which sloughed away entirely. This was thought to have been due to tying of the bronchial artery at the time of the operation. Several operations were done to relieve the symptoms arising from the complications. Incidentally, the patient developed club fingers, but the author pointed out that this was due not to the tumor but to the complications in the lungs.

The gross specimen measured 17 by 12 by 8 cm. and was lobulated. The surface of the cut section had a silky sheen and was grayish white. The tumor had a definite capsule, and connective tissue septums could be seen.

Microscopically, the tumor was composed of nerve fibers, the nonmedullated variety predominating, in which there were collections of rather normal-appearing ganglion cells. Some of them, however, had undergone cystic degeneration. The whole was supported by a structure of wide-meshed connective tissue.

Ganglioneuromas arising in the cervical segment have been removed surgically in two cases, those reported by Glinski⁷ and Freund.⁸

6. Brunner, A.: Die erfolgreiche operative Entfernung eines grossen Ganglioneuroms des hintern Mittelfellraumes, *Arch. f. klin. Chir.* **129**:364, 1924.

7. Glinski, S. K.: Ganglioneurom, *abstr., Deutsche med. Wchnschr.* **32**:2044, 1906.

8. Freund, P.: Ein Ganglioneurom des rechten Hals-sympathikus, *Frankfurt. Ztschr. i. Path.* **13**:266, 1913.

Freund's case was that of a boy about 6 years of age who had had a tumor in the right side of the neck for a year. He developed dyspnea three days before admission to the hospital. Operations in both instances were apparently successful.

SUMMARY

A case of ganglioneuroma arising from the thoracic or the cervical segments of the sympathetic system is reported.

The patient was a boy 4 years of age. The duration of the tumor was twenty-two months; that of the acute symptoms, three months. Operation was performed for relief of the tracheal obstruction; the complete removal of the growth was not possible. Complete relief was obtained for sixteen months. Death followed one month after the recurrence of symptoms.

Pathologically, the tumor showed typical ganglion cells in a bed of nonmedullated nerve fibers, some ganglion cells showing cystic degeneration.

VARIATIONS IN THE EXTRAHEPATIC BILIARY TRACT *

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The frequent recourse to surgery for disturbances in the function of the extrahepatic biliary tract makes imperative exact knowledge not only of the normal distribution of the bile ducts but of the variations occasionally encountered in this system.

The literature contains frequent references to this fact, and many cases are reported of injuries to the biliary tract during operation on subjects in whom the arrangement of the bile ducts was atypical. Jacobson¹ reported a case in which he severed the common bile duct during an operation for gallstones, because the cystic duct paralleled the hepatic duct for some distance. Many instances of similar accidents have been reported. Werelius² and Ginsburg and Speese³ reported cases in which transection of the common duct had been caused entirely by an anomalous arrangement of the ducts. Stetten⁴ reported a case in which the hepatic duct was divided instead of the cystic duct because of the parallel arrangement of the two.

Ruge⁵ described the various forms of the biliary tract and classified them under three main types. The first type consisted solely of the normal angular mode of union of the cystic duct with the hepatic duct. The second type of anomaly included those in which the cystic duct paralleled, for a certain distance, the choledochus. The third type included the two arrangements of the cystic duct in which, instead of leading directly into the right side of the hepatic duct, it wound around it, either anteriorly or posteriorly. Eisendrath⁶ (1918 and 1920)

* Submitted for publication, Oct. 16, 1928.

* Work done in the Department of Pathology, University of Oregon.

1. Jacobson, J. H.: Repair and Reconstruction of the Bile Ducts, *Am. J. Obst. & Gynec.* **70**:940, 1914.

2. Werelius, Axel: Accidental Surgical Injuries to the Bile Ducts with Report of a Case, *J. A. M. A.* **68**:1545 (May 26) 1917.

3. Ginsburg, Nathaniel; and Speese, John: Autogenous Fascial Reconstruction of the Bile Duct, *Ann. Surg.* **65**:79, 1917.

4. Stetten, De W.: Anomalous Relations of the Cystic Duct or Gallbladder to the Hepatic Duct, *S. Clin. North America* **3**:539, 1923.

5. Ruge, Ernst: Beiträge zur chirurgischen Anatomie der grossen Gallenwege, *Arch. f. klin. Chir.* **87**:47, 1908.

6. Eisendrath, D. N.: Anomalies of Bile Ducts and Blood Vessels as the Cause of Accidents in Biliary Surgery, *J. A. M. A.* **71**:864 (Sept. 14) 1918; The Clinical Importance of Anatomical Anomalies in Biliary Surgery, *Boston M. & S. J.* **182**:573, 1920.

presented a study of 100 cases in which the variations in the biliary tract and their relations to the vascular system were discussed. He described each type of variation and specifically stated its significance in relation to accidents during operation. Flint⁷ described two cases, noted clinically, of variations in the distribution of the biliary tract. In one, an accessory cystic duct was encountered during operation for gallstones; in the other, in which operation for cholecystitis was carried out, the cystic duct paralleled the choledochus for its entire length and emptied directly and independently into the duodenum. In an embryologic and comparative study of aberrant biliary vesicles in man and other mammals, Boyden⁸ presented valuable data concerning the frequency with which duplication of the gallbladder may be encountered. In studies on 10,000 domestic animals and reports on 19,000 cadavers and patients in hospitals, the incidence varies somewhat as follows: once in 8 cats; once in 28 calves; once in 85 sheep; once in 198 pigs, and once in from 3,000 to 4,000 human beings. Accordingly, such duplication of the biliary vesicle appears to be relatively rare in man.

A variation from the usual distribution of the biliary ducts, however, is common. Therefore, since cholecystectomy is now more common than simple drainage of the gallbladder, a clear understanding of the more common variations in the distribution of the bile ducts is imperative.

DATA OBTAINED DURING DISSECTION OF CADAVERS

In this report, I wish to present the data which were accumulated during careful dissections of fifty-seven cadavers. The material for these dissections was obtained from necropsies performed for the coroner in Portland, Oregon, and the study was made in the laboratories of the Department of Pathology, the University of Oregon Medical School.

The extrahepatic tracts of the fifty-seven subjects which came under my observation in this study fall into four rather distinct groups. I was able to demonstrate the three types of distribution as described by Ruge and in general to confirm his observations as to the frequency of these variations. The first group of cases, those in which the angular mode of union maintains between the cystic and hepatic ducts constituted 58 per cent of all the dissections (fig. 1 a).

I have subdivided Ruge's second group of variations, those in which the cystic duct coursed parallel to the common bile duct, by arbitrarily

7. Flint, E. R.: Gallstones Associated with Anomaly or Injury of Bile Ducts, *Brit. M. J.* **1**:995, 1924.

8. Boyden, E. A.: The Accessory Gallbladder; an Embryological and Comparative Study of Aberrant Biliary Vesicles Occurring in Man and the Domestic Mammals, *Am. J. Anat.* **38**:177, 1926.

classifying the cystic ducts into two groups on the basis of their length. Furthermore, although the two ducts concerned are bound together in a fibrous union, their lumens are separate. Therefore, it seems better to speak of the cystic duct as running parallel to the hepatic duct and not to the common duct. I have designated the cystic ducts which

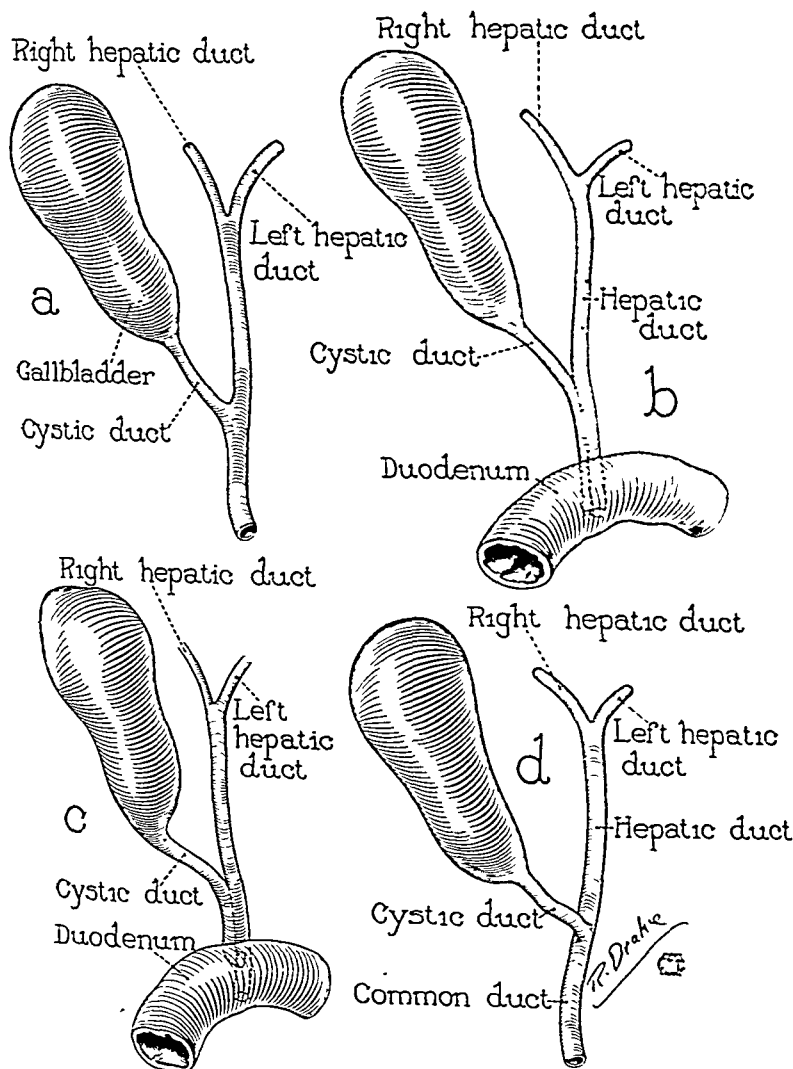


Fig. 1.—Mode of union of cystic and hepatic ducts: *a*, normal angular; *b*, long parallel; *c*, short parallel, and *d*, anterior spiral.

follow the hepatic bile duct as far as the upper border of the duodenum, as the short parallel type (fig. 1 *c*), and I have designated the ducts which extend farther, to within 1 cm. of the ampulla of Vater, as the long parallel type (fig. 1 *b*). In both of these types, however, the cystic and the hepatic ducts are bound together so intimately by fibrous connective tissue that it is almost impossible to separate them. In this

series, 26.3 per cent of the ducts were of the short parallel type and 7 per cent were of the long parallel type. The delayed juncture of the cystic and hepatic ducts, as in these variations, results in a greatly lengthened cystic duct and a relatively short common bile duct. In these aberrant cystic ducts, however, the valves were restricted to the

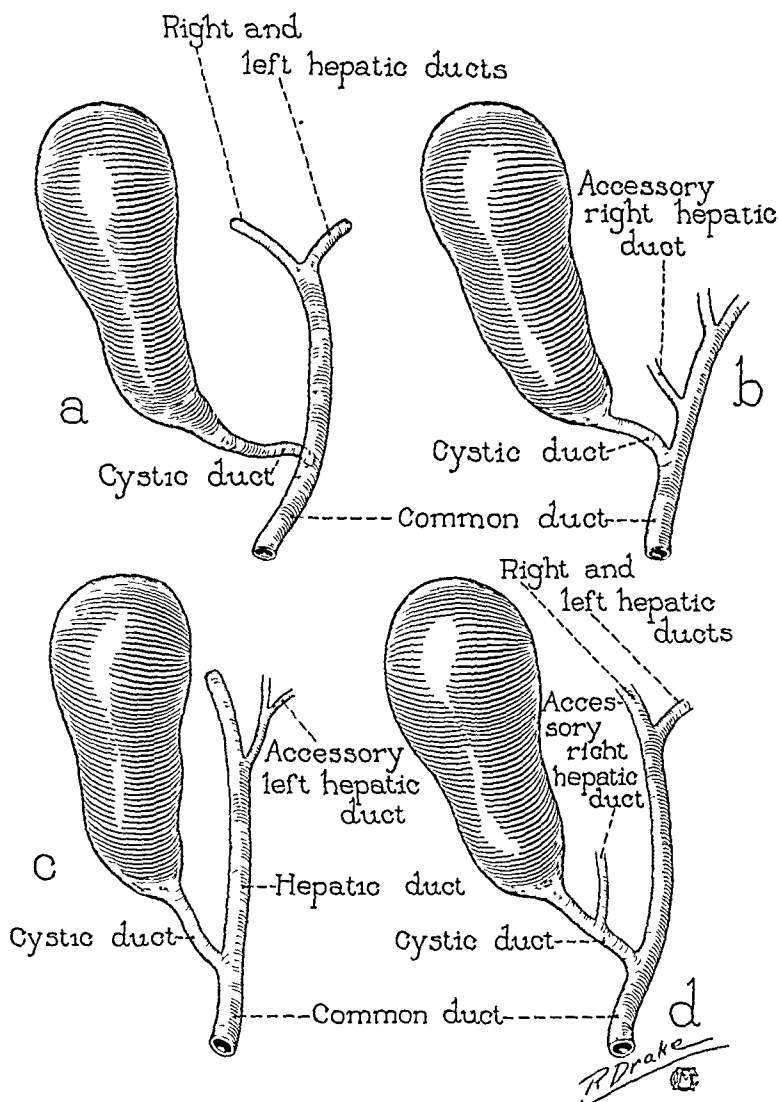


Fig. 2.—a, posterior, spiral mode of union of cystic and hepatic ducts; b, accessory right hepatic duct; c, accessory left hepatic duct, and d, accessory right hepatic duct emptying into the cystic duct.

normal site, for the remaining portion parallel to the hepatic duct was invariably patent throughout.

Of all the cases that came under my observation, 12.3 per cent could be placed in Ruge's third group, the group which includes the anterior and the posterior cystic ducts. In these variations the cystic

duct passes either anteriorly or posteriorly around the hepatic duct, describing from a quarter to a full turn around it. In my series, 7 per cent of the cases were of this anterior spiral variation (fig. 1 *d*) and 5.3 per cent were of the posterior spiral type (fig. 2 *a*).

To these three main types of anomalies, I have added a fourth, which includes variations in the distribution of accessory ducts. The first of these is an accessory hepatic duct which courses from the liver at the extreme right of the portal fissure and empties into the extra-hepatic biliary tract anywhere between the point of confluence of the right and left hepatic ducts and the orifice of the cystic duct (fig. 2 *b*). This particular type of accessory hepatic duct has been hitherto described, but these accessory ducts have been found in the right side of the liver only. In my series a second accessory variation was occasionally encountered (fig. 2 *c*). This duct leaves the liver at the left of the portal fissure and empties into the left hepatic duct before the latter joins the right hepatic duct to form the main hepatic bile duct. As far as I have been able to determine, this left accessory hepatic duct has never been described before. Accessory hepatic ducts, both right and left, were encountered in 3.5 per cent of all subjects examined.

Furthermore, an additional type of accessory duct was encountered in 5.3 per cent of all cases. This duct leaves the liver on the right side of the portal fissure and enters into the cystic duct, instead of into the hepatic duct, just above the confluence of the cystic duct with the hepatic duct (fig. 2 *d*).

SUMMARY AND CONCLUSIONS

1. The normal angular mode of juncture of the cystic duct with the hepatic duct, as described in textbooks of anatomy, occurred in only a little more than half of the cases (58 per cent).

2. The long and short parallel types of cystic duct occur in more than a third of the cases and, as is shown by the literature, is perhaps the most common cause of accidents in biliary surgery. In such cases, there is a marked increase in the length of the cystic duct and a corresponding decrease in that of the common bile duct. The cystic duct and the hepatic duct are so intimately bound together by fibrous tissue that they are absolutely inseparable and thus appear as a single duct; any rough manipulation may tear the thin septum which exists between them. The large portion of a cystic duct of this type which remains following cholecystectomy may dilate and form a new gallbladder, probably with recurrence of symptoms. The cystic duct does not contain valves of Heister in the portion which lies parallel to the hepatic duct. The short parallel type occurred in 26.3 per cent of the cases in this series and the long parallel type in 7 per cent.

3. The anterior and posterior spiral varieties comprised 12 per cent of this series. The length in the anterior spiral variety conforms closely to the normal; in the posterior spiral variety the cystic duct is markedly lengthened, and the hepatic and common ducts remain about normal. It has been recorded that strong traction on the gallbladder is much more likely to tear off a spiral cystic duct than a duct with a normal arrangement.

4. Accessory hepatic ducts occurred in five cases, or 8.7 per cent of this series. Four of these were accessory right hepatic ducts, three of which were also accessory to the cystic duct. In one case there was an accessory left hepatic duct. The length and diameter of the accessory ducts corresponded closely to the normal cystic duct.

A REVIEW OF UROLOGIC SURGERY*

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KIDNEY

Surgical Technic.—Deming¹ reported a study to determine the freedom of incisions about the pelvis and the relative significance of the adjacent vessels which might be cut or ligated accidentally or purposely. He observed that following elongation of the pyelotomy incision straight on to the kidney and to the lower pole the renal circulation is not impaired if the retropelvic vessels are conserved. Angulated incisions cause definite shrinkage of the kidney. The incision of choice is the elongated incision to the lower pole near the median line. The suture of the wound in the kidney should not include any of the larger vessels. Ligation of the retropelvic vessels causes considerable renal injury which is not easily repaired in a few months' time.

Tumors.—Martin² stated that tumors of the kidney fall into three groups, the chief of which consists of growths arising in the renal epithelium. Tumors of connective tissue origin are represented by sarcoma, and the third group is that of the mixed tumor.

Epithelial tumors may originate from three types of epithelium. From the epithelium of the renal tubules, adenomas and carcinomas arise. Papillomas and papillary tumors spring from the epithelium lining the pelvis and calices. The hypernephroma, or third type, arises from suprarenal rests included in the kidney during development.

* Submitted for publication, May 10, 1929.

1. Deming, C. L.: Renal Circulation Following Various Types of Elongations of Pyelotomy Incisions, *J. Urol.* **20**:713, 1928.

2. Martin, E. K.: Tumors of the Kidney, *Brit. J. Surg.* **16**, suppl. no. 13:297, 1928.

Small adenomas not infrequently occur in the cortex of sclerotic kidneys. A single adenoma may arise in an otherwise normal kidney and grow so as to form a clinically recognizable tumor. Adenoma of the kidney, although originally benign, may become malignant.

Carcinoma of the substance of the kidney is more common in men than in women and is not especially associated with the presence of calculus. Grossly, the tumor may appear as a solid, white, infiltrating growth, which destroys and replaces the kidney without appreciably altering either its size or shape. Microscopically, this tumor is frequently a tubular adenocarcinoma, which reproduces the appearance of renal tubules.

The most common form of malignant disease of the kidney is a lobulated and encapsulated adenoma which is yellow or orange and which is often broken up by areas of necrosis and hemorrhage, as well as by the fibrous intersections between its lobules. Microscopically, a hypernephroma is composed of columns of large polyhedral cells, separated from one another by delicate connective tissue carrying thin-walled capillaries. The cells have a clear protoplasm containing fat. Parts of the tumor frequently show a compressed papillary arrangement of the cells in the columns. An exact line of demarcation between the hypernephroma and the papillary carcinoma has not been drawn.

Mixed tumors present a characteristic picture. They occur within the first three years of life, grow rapidly to a large size, and are uniformly fatal. In the early stage they are solid, opaque white, and clearly separated from the substance of the kidney. As they increase in size they may become cystic, and areas of necrosis and hemorrhage may develop. The microscopic structure is that of spindle cells in which are embedded imperfect tubules of columnar epithelium. Tracts of smooth or striated muscle are common, and other mesoblastic tissues, such as cartilage and elastic tissue, are sometimes represented.

Papilloma is a simple tumor with a marked tendency to recur and to take on malignant characteristics. Obstruction of the ureter by these tumors may cause hydronephrosis. Microscopically and grossly, the papillary character of the growth is confined to the surface. In the deeper part of the malignant tumors which infiltrate the kidney, the carcinoma is diffuse.

Sarcoma rarely occurs in the kidney in adult life.

A case of cystic adenoma of the kidney is reported. A large part of the kidney was occupied by an almost spherical tumor, which was composed of brownish material and which had been broken up by hemorrhage and necrosis. The growth was confined within a fibrous capsule and microscopically was an adenoma.

In a second case of adenoma of the kidney, the gross structure markedly resembled a polycystic kidney. The upper half of the kidney

was apparently normal. The renal capsule enclosed the growth, which was sharply demarcated from the substance of the kidney. The tumor was composed of cysts of various sizes, the largest being about 6 cm. in diameter, and the smallest almost microscopic in size.

Another interesting case is that of a papillary carcinoma occurring in one of the calices in a hydronephrotic kidney. The pelvis and calices were distended, and the renal tissue was greatly reduced. The growth occupied one of the lower calices, had infiltrated the surrounding substance of the kidney, and was visible on the surface of the organ. Microscopic examination disclosed squamous cell carcinoma.

Deming³ reported a case of sarcoma of the kidney in a boy, aged 29 days. Nephrectomy was performed under local anesthesia. The tumor was so large that approach was made through an incision in the right rectus muscle extending from the costal margin to the pelvis. The muscles were separated and the peritoneum was opened, exposing the tumor which extended from the liver above, being overlapped by it, to the pelvis below and to the umbilicus mesially. It was adherent above to the liver and the gallbladder, mesially to the ascending colon, and at its lower pole to the cecum and appendix. The adhesions were carefully freed, and the tumor was mobilized. But, as it was otherwise impossible to demonstrate the pedicle, the cyst was tapped, and about 100 cc. of blood and gelatinous fluid was aspirated. The pedicle was then clamped and ligated. The wound was closed in layers, with a small rubber tissue drain inserted at the lower angle. The patient withstood the procedure well, manifesting shock only when the pedicle was being held tense. He recovered readily from the operation and was well six and a half years later. Pathologic diagnosis was congenital spindle cell sarcoma of the kidney.

[COMPILER'S NOTE: The rarity of complete cure of sarcoma of the kidney in a young child makes this case of interest. The majority of cases of tumors of the kidney occurs in the first two years of life. Rarely is one seen and the patient operated on at such an early stage as that reported by Deming. Tumors are generally confined by the renal capsule. They may occur in any part of the kidney and generally involve the entire organ. Metastasis is uncommon and when it does occur is generally in the late stages. If metastasis or local extension has occurred, operation is often followed by a rapidly fatal outcome. Nephrectomy in most cases prolongs life and offers the patient the only chance of improvement. Earlier writers agree on the high mortality. Newer methods of surgical approach, improved asepsis, and at times avoidance of the peritoneal cavity have in most instances greatly

3. Deming, C. L.: Sarcoma of Kidney; Cured, *New England J. Med.* 199: 273, 1928.

reduced the older mortality figures, but definite cures, such as the one cited here, are few.]

Beer⁴ found it necessary to perform nephrectomy in 18 per cent of 271 cases of stone in the kidney in which renal tissue was destroyed. Pyelotomy, with or without nephrotomy, was the procedure of choice in the remainder of the cases. In 29 of the last 38 cases, he performed pyelolithotomy and in 1, wide nephrolithotomy. The increased use of pyelolithotomy was due to the fact that it saves the parenchyma of the kidney and assures complete removal of all calculous material. It may also be used in cases of complicated stones.

If the kidney cannot be delivered and it is necessary to perform nephrotomy, Beer performed a bloodless operation by placing a rubber tourniquet around the pedicle. In all cases he followed the principles of constricting the ureter to prevent fragments from falling into it and of having the roentgenograms of the kidney developed immediately after removal of the stones. In about fifteen cases of stones of complicated shape, fragments were still present but were easily located and removed.

Randall⁵ stated that there are three prevailing theories regarding the etiology of formation of stone. The first is the action of specific bacteria. The second is based on colloidal chemistry, beginning with the facts that calculi result from an abnormal type of crystalline precipitation, that normal urine holds water-insoluble crystalloids in solution because of the presence of protective colloids, that hydrogen ion concentration affects this solution, and that the colloidal matter in solution modifies the morphology of crystalline precipitates. Basing his experiment on these factors, Keyser produced calculi by disturbing the urinary colloidal balance. He concluded that this disturbance may be due to quantitative changes in the colloids normally present, or to the entrance of abnormal colloids into the urine, either from the blood stream or as products of local renal disease. The frequency of formation of stones in animals having a diet deficient in vitamin A is the basis for the third theory. Such calculi consist essentially of the characteristic insoluble phosphates of calcium and magnesium, and treatment by dietary measures has resulted in the successful disappearance of these stones.

In from 3 to 81 per cent of the cases, the nucleus of stones was composed of urates and uric acid. Oxalates were present in ratios from 5 to 66 per cent.

Randall expressed the belief that vesical calculi are uniformly secondary formations to foreign bodies, to vesical obstructions causing

4. Beer, Edwin: *Bemerkungen über die Technik der operativen Entfernung von Nierensteinen*, *Ztschr. f. urol. Chir.* **24**:601, 1928.

5. Randall, Alexander: *Rapidity of Growth of Urinary Calculi*, *Atlantic M. J.* **31**:937, 1928.

residual urine, to vesical diverticula, to renal lesions and to descending stones. Incomplete prostatic operation which prevents complete emptying of the bladder often predisposes to secondary formation of stones. It is recognized that phosphatic stones grow more rapidly than others and that their growth is markedly influenced by the presence of a foreign body or alkaline cystitis.

Randall reported the growth of a stone in one of his patients who had taken some pills containing methylene blue (methylthionine chloride, U. S. P.) for urinary trouble. At operation three years later, two calculi measuring 3 by 2.5 by 1.5 cm. were removed. On section, each appeared to be formed of pure ammonium urate; the laminae in the early growths were stained green, showing a growth of 2 cm. in the three year interval. In another of Randall's cases three stones were removed from the bladder, the largest measuring 4 by 3 by 2 cm. The growth, in eighteen months, was due to alkaline cystitis and a contracted vesical orifice. In a museum is displayed a string of four calculi, the largest measuring 3 by 3 by 2 cm., all adherent to a linen thread, which probably had been misapplied during herniotomy five months before.

Nay⁶ stated that renal stones should be considered recurrent only when proved not to have been overlooked. He expressed the belief that infection is the cause of calculi in a large number of cases. Preoperative treatment should consist of removal of the focal infection, if possible, and treatment of the kidney. Postoperative treatment is important because it helps to reduce the recurrence of stones by leaving the patient with a good uninfected kidney.

Herbst, in discussing the recurrence of stone in the kidney, considered that focal infections play only a small part in the cause and recurrence of lithiasis. It is his belief that renal retention and infection are the important factors in the production and reappearance of renal calculi, and that the correction of these conditions following removal will reduce the number of recurrences.

Mattes⁷ stated that urolithiasis is considered of rare occurrence in the colored race. In 1913, Pfister reviewed the literature and noted particularly the occurrence of renal stone in the colored people of Africa, South America and the German colonies. He observed that the appearance of calculi depends on the locality, the soil and the water, and that in some regions it is almost unknown. Pfister stated the belief that if the examination of the two races was equally thorough, stone would be found as frequently in the colored as in the white race. Mattes' figures show that there was three colored persons with stone to seven white in 1924, and in 1925 he noted a ratio of one colored to five white persons.

6. Nay, E. O.: Prevention of Recurrent Renal Calculi, *J. Urol.* 20:553, 1928.

7. Mattes, A.: Renal Calculi in the Colored, *South. M. J.* 20:941, 1927; abstr., *Ztschr. f. urol. Chir.* 24:408, 1928.

Walthers stated that formation of stone in the negro was rare and that he had seen few cases. During a period of ten to twelve years in a hospital for the colored, Righton never observed stones although many roentgen examinations were made. Hayes did not observe a single case in three years. Many other urologists, among them Kelly, who sees a great many negro patients, report similar experiences.

Ray⁸ stated that urinary calculi commonly consist of certain substances insoluble in water and urine. Crystals of these substances are sometimes found in normal urine, but they are generally isolated and single. These particles may be held in solution, may deposit a fine sediment, or may form calculi, and are brought about by colloidal substance. Ray believed that the absence of colloids in the urine is brought about by certain pathologic conditions within the kidney, due either to local disease or to outside influences reacting on the organ.

Billington⁹ attempted to assess the value of the results of nephropexy. He considered it from two aspects: (1) the surgical success of the operation permanently replacing the kidneys in their normal position without unsatisfactory sequelae, such as pain in the loin or back, hernia of the wound and persistent sinus, and (2) its therapeutic value in curing or ameliorating the symptoms for which it is performed. At first the results were not satisfactory. In a large percentage of cases the operation failed to cure the abnormal mobility of the kidneys, and they were found loose again as soon as active life was resumed. Many operations fixed the kidney to the muscles of the back at too low a level, with the result that pain in the back was common and at times hydronephrosis developed. The use of silk and other nonabsorbable suture materials was followed by persistent sinuses, and extensive injury to the muscles of the loin led to a feeling of weakness and hernia. A further and common cause of failure is the incomplete character of the operation. One kidney only is replaced, while the other one, which may also be mobile, and a possibly diseased appendix are left untreated. Only when the surgeon is satisfied that both kidneys are in a normal position and that associated or secondary abdominal lesions may have been excluded or treated can success be claimed.

Billington has performed nephropexy on 1,500 patients, and it has been his object to replace both kidneys, if necessary, and to make sure that intra-abdominal lesions were not left undetected and untreated. The surgical results were satisfactory; in not a single instance has he found a kidney loose again. Of 163 patients who were traced, 71 (43.6 per cent) reported that the operation was successful, 41 (25 per cent)

8. Ray, D. P.: *Etiology of Urinary Calculi*, *Atlantic M. J.* **31**:934, 1928.

9. Billington, William: *The Therapeutic Value of Nephropexy*, *Brit. M. J.* **2**:975, 1928.

reported that it was partially successful, usually indicating relief of renal symptoms but not all associated symptoms, and 51 (31.4 per cent) reported failure.

Pylonephritis.—LeComte¹⁰ discussed the anatomic changes brought about by pregnancy and their influence on renal drainage. It is a well-established principle of urinary lesions that any obstruction will sooner or later cause infection; its duration will depend on the degree of obstruction, and the extent of injury will depend on the length of time it is permitted to act. A second principle is that the hazard to the integrity of the kidney is in proportion to the distance that the obstruction occurs from it. Frequent painful urination and pyuria should be considered as indications of a possible serious infection of the kidney.

During pregnancy, the form of the urinary organs is changed and function is disturbed by the enlarging uterus. The urethra is elongated early and the bladder is soon compressed and drawn upward, so that by the third month it becomes an abdominal organ. Functionally, these changes lead to frequency and residual urine, with the common sequence of bacteriuria and inflammation. Sluggish peristalsis was noted in 80 of 100 normal pregnant women on whom cystoscopy was performed. The abdominal ureter and renal pelvis are commonly found dilated during pregnancy. Varying degrees of dilatation were noted in all normal pregnant and parturient women who were submitted to pyelography; all presented symptoms of renal pain, or infection was present. While changes are taking place in the lower tract, the ureters and renal pelves are being slowly dilated by the intermittent obstruction afforded by the enlarged uterus. In some cases, due to the patient's high resistance or the absence of bacteria specific for the tissues at hand, the process stops; in others, inflammation results. Occasionally a vicious circle is established, the bladder becoming infected and the kidneys becoming reinfected from the bladder, this infection occurring either from the blood stream or ascending along the lymphatics of the ureter. If these changes occur early in pregnancy and are not relieved by treatment, the fetus usually dies from the infectious toxemia and the uterus empties spontaneously.

LeComte stated the belief that the greatest aid in the recovery of an infected kidney is the establishment of free drainage. During pregnancy, this may be brought about independent of whatever treatment is given and may lead to a good result. In the way of treatment, rest in bed during the febrile intervals is indicated, and the patient should lie on the side opposite that infected as much as possible, in order to relieve the pressure of the uterus on the ureter by gravity.

10. LeComte, R. M.: *Kidney Infections During Pregnancy*, Virginia M. Monthly 55:481, 1928.

Duncan and Seng¹¹ reported a survey of the protective mechanism of the urinary tract of healthy pregnant and puerperal women. They observed that physiologic forces external to the ureter cause obstruction to ureteral and renal drainage in pregnancy, which is relieved almost immediately on termination of gestation. Right-sided ureteral dilatation is constantly present; hydronephrosis on the right occurs only slightly less frequently. The left ureter and renal pelvis escape this dilatation in a high percentage of cases. Bilateral hydro-ureter and hydronephrosis were of common occurrence, and were apparent earlier, more frequently and in more marked degree in the multipara than in the primipara.

Stasis, as measured by inability of the renal pelvis and ureters to empty themselves within the normal time limits, is definitely and almost universally observed in women before delivery. It is still persistent in a less degree over a prolonged period after delivery.

Duncan and Seng demonstrated an unexpected amount of pus and coliform organisms in specimens from the bladder and kidney of supposedly healthy pregnant women and in women after delivery. They concluded that every pregnant woman has some degree of obstruction, definite dilatation of the ureters and renal pelvises, and well defined stasis continuing over a long period. They further demonstrated that in the apparently healthy pregnant and puerperal patients there is a probable renal complication, the presence of pus and coliform organisms. The line of demarcation between the physiologic and pathologic conditions in these cases is fine. These authors expressed the belief that these women are all subjects for potential pyelitis.

Blanton¹² stated that pyelitis is the most common urologic disturbance found during early life. It may arise as a primary infection but usually follows some other acute infection, such as tonsillitis, bronchitis or pneumonia. As a primary disease it is usually present during the early months of life, and mainly in girls, as a result of the proximity of the urethral opening and the anus and also of the short urethra in the female. It is caused chiefly by the colon bacillus and tends to be an ascending infection, the bacilli traveling up through the urethra and bladder to the pelvis of the kidney by way of the ureter or lymphatics. It may also be due to direct extension of infection from some nearby organ, such as the appendix or other portion of the intestinal tract. When it results from a hematogenous infection, the causative organisms are carried from some distant focus to the renal pelvis, where inflammation occurs. Any obstruction to the urinary flow from the kidney

11. Duncan, J. W., and Seng, M. I.: Factors Predisposing to Pyelitis in Pregnancy, *Am. J. Obst. & Gynec.* **16**:557, 1928.

12. Blanton, J. L.: Pyelitis of Infancy and Childhood, *Virginia M. Monthly* **55**:479, 1928.

predisposes to infection. The common causative organisms, in their order of frequency, are the colon bacillus, *Staphylococcus albus* and *Staphylococcus aureus*, the streptococcus, the typhoid bacillus, the pneumococcus and *Bacillus pyocyaneus*.

The acute form of pyelitis is characterized by sudden onset, frequently with a chill, followed by high fever and sweating. Chronic pyelitis may follow the acute form, or it may arise as a complication of some other disease and pass unrecognized unless discovered by urinalysis. It may exist for months or even years without causing typical symptoms.

Alkalis or antiseptics may be used in the treatment for acute pyelitis. The alkaline treatment is indicated in those cases in which the urine is acid, small in quantity and full of pus cells. Some alkaline diuretic, such as potassium citrate or acetate, or a combination of alkaline diuretics, should be used and fluids forced. If the pyuria is not cleared up promptly by this method, Blanton uses the antiseptic treatment, which tends to make the urine sterile. The common antiseptic used is hexamethylenamine or methenamine. He considers the cystoscope an aid in the treatment of many patients, even young children. The attempt should be made to eliminate all obstruction to the urinary flow and to treat the condition locally by means of lavage with antiseptic solutions; this is often successful when medical treatment fails.

Tuberculosis.—Greifenstein and Kehl¹³ reported forty-three nephrectomies for renal tuberculosis performed at the surgical clinic of the University of Marburg between 1891 and 1923. A follow-up study was possible in forty-one cases. The period of operative mortality extended from one to six months. In a second danger period of from one to three years, deaths caused by tuberculous complication occurred. Thirteen patients died. This high mortality was due to the primitive diagnoses and treatment of the earlier period. Histologic studies frequently disclosed bilateral renal tuberculosis when clinical proof was lacking. The mode of infection of the second kidney was the same as that of the first, namely, hematogenous. Infection by the urinary route can occur only in cases of advanced tuberculosis of the bladder.

The follow-up study of cases in which nephrectomy was done revealed that the patients remained tuberculous and succumbed sooner or later to tuberculosis. The prognosis appears more favorable in women. In men, genital tuberculosis does not exert any greater influence on the prognosis than that of any other organ, provided it is not complicated by active pulmonary tuberculosis. Of thirteen patients

13. Greifenstein, A., and Kehl, H.: Die Ergebnisse der Behandlung der Nierentuberkulose in der chirurgischen Klinik zu Marburg, Deutsche Ztschr. f. Chir. 208:1, 1928.

living, eight were entirely cured, four were improved, and one was worse. Injury to the peritoneum during nephrectomy on the right side rarely resulted in peritonitis. On the other hand, infection of the wound and the formation of fistula occurred in 17 per cent of the cases. The method of treating the stump of the ureter did not seem to be of any significance in this connection. The fistulas healed, as a rule. Nonsurgical treatment of renal tuberculosis is not to be considered, although in rare cases cure is possible through complete destruction of the organ in the absence of all symptoms.

Scholefield¹⁴ reported seventy-four cases of renal tuberculosis with fifty-nine nephrectomies from the Peter Bent Brigham Hospital. Two patients died within the first few weeks after the operation, and six died after a few years. Eighteen of the patients traced are known to be alive and well more than three years after the operation, while only eight are known to have continued symptoms of urinary tuberculosis. The remaining twenty-five were observed recently, or were lost track of before the end of three years.

Of the fifty-seven patients leaving the hospital, twenty-three (40 per cent) reported primary healing of the lesions, which remained healed. In twenty-four cases (42 per cent) sinuses developed which required attention for from three months to several years.

Scholefield concluded that in cases in which, at operation, the kidneys appeared little diseased sinuses were more apt to occur than in those in which extensive caseation was present. Involvement of the ureter or of the perinephric fat did not seem to have any bearing on the healing of the wound. The average period during which symptoms had been present was twenty-eight and six-tenths months in cases in which lesions healed, and sixteen and three-tenths months in those in which sinuses developed. The more acute the process, therefore, the more likelihood there is for the development of a sinus. Scholefield suggested that these sinuses are due not to the continuation of any existing infection but to the development of a new tuberculous process in the traumatized tissues of a patient whose resistance is lowered.

Cathelin¹⁵ stated that the dictum of Albarran that early nephrectomy is essential in renal tuberculosis still holds good. He discussed several complications following the removal of tuberculous kidneys.

Lumbar fistula is a commonly observed sequel after renal tuberculosis. Twenty or thirty years ago, fistulas were common, but today, with the present methods of surgical technic, they are fewer. So-called

14. Scholefield, B. G.: *Renal Tuberculosis: Healing of Tuberculous Nephrectomy Wounds*, J. Urol. **20**:345, 1928.

15. Cathelin, F.: *Les séquelles de néphrectomie pour tuberculose rénale*, Rev. gén. de clin. et de thérap. **42**:321, 1928.

urétéraux forcés, or dilated ureteral orifices, with urinary reflux, are rare at the present time.

Cathelin reviewed the histories in forty-five cases of nephrectomy. In most of them the lesions healed in from five to ten months, and in the majority of the remainder, in from ten to sixteen months after operation. In three of the cases the condition lasted for from eighteen to twenty-two months; in one for twenty-four months, and in another for thirty-one months. Cathelin follows two primary rules: he never washes the wound, and touches the base of the wound as little as possible. Reopening of the wound occurred in fifty of Cathelin's cases.

Occasionally there is considerable pain in the remaining kidney, due usually to hypersecretion and hyperfunction. This painful phenomenon is usually explained by simple reflex excitations and intermittent congestion.

Continuation of the symptoms in the bladder occurs in about 50 per cent of the cases. In half of these there is no change following operation, and in the other half there is moderate amelioration. In the remaining 50 per cent of the cases, the condition clears up completely. Cathelin uses oil of gomenol, 10 per cent strength, injecting 5 cc. every second day. On alternate days bladder lavage is carried out.

Fronstein¹⁶ stated that 80 per cent of patients with renal tuberculosis who are treated by conservative methods die in the course of five years after the onset of the disease. After ten years, practically none is living. On the other hand, about 75 per cent of patients operated on live their normal span of life. The postoperative results vary directly with the length of time the symptoms have been present preoperatively. The earlier the diagnosis and operation, the more satisfactory the results. One of the significant diagnostic points is the finding of bacilli of tuberculosis in the urine. Albuminuria is also of significance. Fedoroff observed albuminuria in 85 per cent of his cases. In Fronstein's series, it occurred in all cases. Dysuria is an early symptom and occurs in 94 per cent of the cases. Pyelography is of exceptional value in diagnosis.

Fain¹⁷ stated that while the bacillus of tuberculosis causes specific changes, it may at the same time bring about nonspecific nephritis, nephrosis and cirrhotic changes. In such a tuberculous kidney, tubercle formation is frequently not to be discovered. The course of a non-specific renal change may be slow and end with contraction. With non-specific tuberculous nephritis there may also be specific changes, and for that reason the diagnosis may be undetermined in each case. The pathologic-anatomic mutations show the frequency of bilateral tuber-

16. Fronstein, R.: Le diagnostic de la tuberculose rénale, *J. d'urol.* **25**:434, 1928.

17. Fain, L.: Ueber die Frühdiagnose und Therapie der Initial formen der Tuberkulose der Harnorgane, *Ztschr. f. urol. Chir.* **24**:421, 1928.

culous nephritis. Clinically, the differential diagnosis of tuberculous nephritis and tuberculous bacilluria is quite difficult and sometimes impossible, especially if there is a history of a common disease of the kidney. The difficulty in diagnosis is due to the similarity of the clinical manifestations of these diseases, which necessitate long observation and repeated examinations of the patient. In nonspecific renal changes associated with a tuberculous bacilluria or tuberculous nephritis, the absence of pyuria or the presence of slight or easily treated pyuria of the pelvis is characteristic; at the same time, the cystitis is of the non-ulcerative type and treatment is carried out in the usual manner, with relief. The additional renal pyuria which does not yield to the customary treatment, associated with severe cystitis and diminution in renal function, shows in most cases a destructive renal tuberculous infection. In the event of operative treatment for nonspecific infections of the kidneys which permit the passage of bacilli of tuberculosis, or in kidneys showing tuberculous nephritis, it is advisable to use some conservative procedures, such as decapsulation, nephrotomy, pyelotomy or ureterotomy. Such patients must remain under constant observation, since the kidney operated on conservatively is in continual danger of undergoing tuberculous changes and necrosis.

Cystic Disease.—Crosbie¹⁸ stated that large solitary cysts of the kidney should not be confused with smaller cysts occurring in nephritis and in sclerotic kidneys. Large cysts are usually unilateral and never connect with the renal pelvis, and the remaining renal tissue is as a rule normal. The cyst is usually situated at one pole of the kidney. It is more common in woman than in man, and the fluid is clear, straw-colored and rarely bloody. Symptoms are referable to the pressure of the cyst either on the remaining part of the kidney or on other organs. Hematuria is rare.

Treatment is operative. If the cyst is situated at one pole, it may be possible to do a resection and save the remainder of the kidney. Crosbie reported the case of a large cyst in the median portion of the kidney, in which nephrectomy was performed. On section the cyst was found to be lined by smooth, shiny, glistening tissue. There was an incomplete septum which partially lobulated the cyst. The fluid content was pale and clear, and there was no evidence of infection.

Barney, in discussing Crosbie's paper, reported a case of renal cyst in which the main symptoms were hematuria and retention of urine. At operation the kidney seemed to be in good condition elsewhere, so he trimmed off the cyst at its juncture with the cortex. In an effort to

18. Crosbie, A. H.: Solitary Cyst of the Kidney, *New England J. Med.* **199**: 277, 1928.

dissect out the lining membrane of the cyst from the cortex, he encountered considerable bleeding, so instead the cavity was swabbed out with Zenker's fluid.

Blood Supply.—Ferrer¹⁹ stated that distention of the renal pelvis and calices to their normal capacity will produce distinct, partial obstruction to the outflow of venous blood in the kidney, which is proportionate to the degree of distention. Any obstruction to the free outflow from the renal pelvis will tend to produce renal passive congestion, and a continuously distended pelvis may aid in the formation of hydronephrosis.

Ferrer expressed the belief that pyelovenous backflow is only a temporary phenomenon, and will persist only as long as the venous outflow fails to increase in pressure sufficiently to overpower that of the backflow. A more complete understanding of this type of obstruction will lead to better use of a permanent catheter, or at least of ureteral drainage and dilatation in many of the obstructive uropathic conditions encountered, especially in pregnancy. Pyelography should be done with care, and there should be a tendency to rely more on small amounts of concentrated solution than on weak but larger amounts of fluid.

Renal Reflexes.—Papin²⁰ stated that the nerve tracts of the kidney and its pelves carry two types of fibers, sensory and vasomotor, and that there are two types of reflexes, plain and secretory. Only the normal kidney is the seat of pain sensations. One of Papin's cases is illustrative of this. There was severe pain in the left loin due to right-sided hydronephrosis. Following removal of this lesion, the pain in the left kidney disappeared. Up to the present, observations show that the reflex pain in the normal kidney more often is associated with nephrolithiasis and less frequently with movable kidney, hydronephrosis, pyelitis, tuberculosis and renal tumors.

In the involvement of the kidney, and especially of the renal pelvis, the pain is not precipitated in the organ itself, but is referred to the corresponding Head's area on the surface of the body, usually on the same side; occasionally it is referred to both sides and in rare cases to the opposite side.

The problem of reflex secretory disturbances is still far from being clearly understood. Its manifestations are oliguria and, in rare cases, polyuria. Clinical observation has shown the following types: fatal anuria in unilateral obstruction; oliguria in a unilateral lesion, which

19. Ferrer, J. C.: Obstruction to the Venous Circulation in the Kidney Caused by Distention of the Pelvis and Calices, with Special Reference to Pyelovenous Backflow, *J. Urol.* **20**:701, 1928.

20. Papin, E.: Actions réflexes réno-rénales, *Arch. d. mal. d. reins* **2**:518, 1927; abstr., *Ztschr. f. urol. Chir.* **24**:335, 1928.

may be aided by removal of the diseased kidney; transient anuria following nephrectomy or a conservative renal operation, and polyuria after nephrectomy. One form of reflex polyuria occurs in tuberculosis, explained by Graser as a reflex of the pathologic conditions of the kidney brought about by vesical pollakiuria. Papin observed true reflex polyuria of the normal kidney in a case in which nephrectomy was done for hydronephrosis associated with infection. Clamps were left in place because of a short pedicle; polyuria developed, the amount of urine reaching 6,000 cc. by the fifth day. Following removal after the clamps were removed, the output diminished to 2,000 cc., where it remained.

Experimentation has not furnished any definite facts. The production of reflex anuria has been successful only in rare cases in which the condition was not clearly defined. The question as to whether anuria can occur in a normal kidney, whether the anuria may be permanent, or whether it disappears with the removal of the cause has not been solved. According to Neuwirth, reflex anuria is brought about through a spastic condition of the intrarenal vessels, which come through the vasomotor paths. This reflex is abolished by a break in the vasomotors (splanchnic anesthesia). Further researches of Neuwirth, and later of Koennekes, have shown that the splanchnic nerves carry not only vasomotor but sensory fibers, afferent and efferent, which can be affected by the same factors.

The question of reflex polyuria is even more doubtful. Experimentally, the only fact proved is that there is a polyuria center in the tuber cinereum of the medulla. Polyuria caused by splanchnic section is only transient, and always involves the same side.

Papin noted that clinical experience has yielded a few facts to explain some of these secretory disturbances. Nephrectomy has usually been difficult, and either the clamps were left on the pedicle or the ligatures had to be applied close to the large vessels. This probably caused direct irritation or destruction of the ganglions in these coursing reflex tracts.

Wounds.—Harris²¹ reported a case of rupture of the kidney which he diagnosed by means of pyelography more than three weeks after the injury. He was impressed by the tremendous recuperative and reparative power of the kidney. He stated the belief that these patients are generally not observed long enough to determine that mechanical defects have not, at a later date, been followed by complicating infection and even by the formation of stone, resulting ultimately in destruction of renal tissue. He drew the following conclusions: ureteropyelographic study should be done in every case of renal trauma, after all acute

21. Harris, A.: Traumatic Rupture of Left Kidney: Case Report, *J. Urol.* 20:193, 1928.

symptoms have subsided. The time to investigate depends on the symptoms in the individual case and the judgment of the surgeon. More complete follow-up study should be carried out over a long period in every case to control secondary complication of infection and the formation of stone as far as possible. Chronic infection without obstruction might continue for long periods without symptoms sufficient to necessitate the consulting of a physician by the patient. Catheterization and renal lavage might be valuable in controlling infection. The reparative power of the kidney is remarkable. Open operation is indicated only in the exceptional, extreme case of renal injury, with uncontrollable hemorrhage. Infection following extravasation of urine or hematoma may require drainage. It is possible that an infected pouch, sinus or sac, not relieved by lavage, might be removed by open operation, the kidney being conserved at the same time. An accessory pouch seen in the pyelogram must be distinguished from solitary cyst of the kidney.

Suprarenal-Renal Heterotopia.—Caylor²² considered suprarenal-renal heterotopia as an anomaly of surgical and general significance, and defined it as the developmental inclusion of the suprarenal gland beneath the capsule of the kidney. Rests of suprarenal tissue are not included in this group, as they are usually made up of cortical cells, in contrast to true heterotopia in which both cortical and medullary elements are present. All or only a part of the suprarenal gland may be beneath the renal capsule.

Caylor found thirteen cases reported in the literature, and he added a fourteenth. A well developed woman, aged 34, apparently in good health, came to the Mayo Clinic for general examination. In the course of the examination, hydronephrosis of the right kidney was discovered. This kidney had a low functional value, while the left kidney functioned normally. The right kidney was removed through a lumbar incision. An accessory vessel to the right kidney was thought to have been a factor in causing the hydronephrosis. The kidney weighed 180 Gm. The hydronephrotic dilatation of the pelvis had apparently destroyed from 30 to 40 per cent of the parenchyma, and the anterior-superior surface of the kidney was partially covered with a yellow plaque, the suprarenal gland. As the capsule was stripped from the kidney, the gland was found intact beneath it, instead of in its usual situation in the perirenal fat. Duplication of the gland was not found.

Postoperative Statistics.—Hunt²³ reviewed the major surgical conditions arising in the kidney in cases observed at the Mayo Clinic during

22. Caylor, H. D.: Suprarenal-Renal Heterotopia: Report of a Case, *J. Urol.* 20:197, 1928.

23. Hunt, V. C.: A Review of the Surgery of the Kidney. *Proc. Staff. Meet. Mayo Clinic* 3:201, 1928.

the last six years. During this period, 1,640 operations were performed on the kidney. Nephrectomy was performed in 1,119 cases (68 per cent). In 157 of the cases, the disease was malignant; 11 patients died following nephrectomy, a mortality of 7 per cent. The remaining 962 nephrectomies were performed for benign disease, with 20 deaths, a mortality rate of 2 per cent. Five hundred and twenty-one conservative operations were performed on the kidney largely for lithiasis, with 8 deaths, a mortality of 1.5 per cent.

Renal stone was the most common surgical lesion, comprising 808 cases (49.2 per cent). Nephrectomy was performed in 287 (35.5 per cent) of the total number of cases of lithiasis. Seven deaths (2.4 per cent) occurred, as opposed to 1.5 per cent for the conservative operation. There were 521 conservative operations, such as pelviolithotomy (85 per cent), nephrolithotomy, or the combined operation.

Nephrectomy was done for renal tuberculosis in 305 cases (27.2 per cent). There were 6 deaths, a mortality of 1.9 per cent. In 336 cases (30 per cent of all the conditions that required nephrectomy) the operation was performed for pyonephrosis, pyelonephritis and hydronephrosis with infection.

One hundred and fifty-seven nephrectomies were performed for malignant disease of the kidney. Hypernephroma was the predominating lesion, occurring in 113 cases (72 per cent of all the malignant lesions); carcinoma, 20 cases (12.7 per cent); epithelioma, 17 cases (10.8 per cent), and sarcoma, 7 cases (4.4 per cent).

Operation was performed in 23 cases of fused or horseshoe kidney. There were 12 cases of renal lithiasis in which the stones were removed by pelviolithotomy.

Heminephrectomy was necessary in 6 cases of hydronephrosis; cysts were drained in 2 cases, exploration for pain was carried out in 2 cases, and accessory vessels were divided in 2 cases.

Braasch, in discussing Hunt's paper, stated that more than 30,000 cystoscopies had been performed during the same period. During these six years, there were a great many more patients with surgical lesions of the kidney who were not operated on for various reasons. Fully a third of the patients came with symptoms not referable to the urinary tract; possible involvement of the kidney was suggested only after careful examination. The mortality rate in nephrectomy performed for renal tuberculosis was 1.9 per cent, which is about the same as that in the total number of cases in which operations were performed on the kidneys.

Wildbolz recently quoted statistics of a series of 640 nephrectomies, showing a mortality of 2.8 per cent. He stated, however, that this number included a series of more than 100 cases in which operation

was performed without a fatality; this is further evidence that statistics based on a small number of cases are without value.

Attention was called to the high percentage of patients with renal lithiasis in whom it was necessary to remove the kidney. Braasch stated that the general practitioner is often largely responsible for this, since if he had insisted on investigating the cause of the patient's colic and if after the diagnosis of stone had been made he had insisted on operation, a conservative operation might have been possible. A conservative operation, of course, is best because of the possibility of bilateral lithiasis, if for no other reason.

URETER

Infection.—Kidd²⁴ suggested that the ureter should be examined carefully before nephrectomy is done, as in selected cases the removal of the major portion of the ureter, besides the kidney, will be found to give better results. In cases of hydronephrosis, if the obstruction of the ureter is in the pelvic region and the ureter as far as the obstruction is not removed, the portion remaining frequently causes trouble. The ureteral stump may remain infected and cause attacks of colic, fever and strangury, or a large infected pouch may form. In some cases, these attacks of dysuria and fever resulting from ureteral retention are relieved by the passage of purulent urine.

Some surgeons remove as large a portion of the ureter as possible when removing a tuberculous kidney; others consider that this step entails risk of the formation of an abscess or urinary fistula deep in the pelvis. Kidd believed that in cases of septic stones impacted in the pelvic ureter with a dilated atrophic ureter above, primary nephro-ureterectomy should be done. If the lumen of the ureter is not obstructed, complications will rarely arise even if the ureter is left in place. The inflamed and infected ureter will gradually atrophy and its contents become sterile. If the process of sterilization is delayed, it can be hastened by washing out the stump of the ureter. Kidd has noted that in many cases after operation for calculous pyonephrosis the stump of the ureter has become aseptic and has not given further trouble. On the other hand, if there is an obstruction between the site of the ligature and the bladder, trouble will probably arise in the stump of the ureter: the muscular wall will hypertrophy in an endeavor to get rid of the contents of the ureter, causing attacks of ureteral colic. The lumen of the ureter may become dilated and cause severe symptoms of urinary infection.

Kidd gave the following indications for primary nephro-ureterectomy: (1) in hydronephrosis, simple or infected, when the stricture is

24. Kidd, Frank: The Stump of the Ureter After Nephrectomy: Indications i - Primary Nephro-Ureterectomy, Brit. J. Surg. 16:22, 1928.

low in the pelvic ureter; (2) in pyonephrosis or atrophic septic or aseptic kidney secondary to a stone long impacted in the pelvic ureter; (3) in tuberculous pyonephrosis associated with inflammatory stricture in the pelvic ureter, and (4) in all other types of pyonephrosis associated with inflammatory stricture in the pelvic ureter.

In most cases in which Kidd performs primary *nephro-ureterectomy* he cuts down on the kidney from behind, and after it has been freed and its pedicle tied, he frees the lumbar ureter from its connections, taking care to tie all bleeding points, which may be numerous. The ureter can be burned across with a cautery, or the kidney and ureter can be left hanging out of the lower margin of the wound, which is then stitched up and the patient turned on his back. In the cases in which operation is more easily performed and in which the obstruction is high in the pelvic ureter, such as a stone, the ureter is then exposed extraperitoneally through a muscle-splitting incision for exposing the pelvic ureter, tied off with catgut below the point of obstruction, burned across, and with the kidney is drawn out from the wound in the back. If a drain is carried to the stump of the pelvic ureter, it should consist of a piece of rubber glove; tubes endanger the walls of the iliac vessels and should not be employed. If, on the other hand, the operation is difficult and the obstruction lies close to or even in the walls of the bladder, a better exposure can be obtained by turning the rectus muscle outward from near the median line below the umbilicus. Through this incision the ureter can be stripped extraperitoneally to the wall of the bladder; the numerous branches of the internal iliac and other vessels running to the wall of the pelvic ureter and bladder can be exposed and tied off, and the ureter can be completely removed. In some cases it has even been found necessary to remove a portion of the wall of the bladder, a step that is feasible through this incision.

Read²⁵ reported a case of empyema of the ureteral stump in a woman, aged 31. One week after hysterectomy, pus appeared in the urine. Three months later, a ureterovaginal fistula was found. The end of the left ureter was located in the fibrous tissue of the pelvis and transplanted into the upper angle of the bladder. The vaginal fistula healed, but foul pyuria persisted, and pain in the lower left quadrant and lower lumbar regions became increasingly severe. Six weeks later the pyuria was more severe, and left nephrectomy was performed. Pathologic examination disclosed general pyonephrosis. Two months after the nephrectomy the patient began to have severe, shooting pains along the course of the left ureter, radiating into the bladder. The attacks came on suddenly and lasted for from two to seven days.

25. Read, J. S.: A Ureteral Stump (Non-Tuberculosis) as a Source of Pyuria: Case Report, *J. Urol.* **21**:103, 1929.

Immediately after a colicky attack there was a large amount of pus in the urine: this was followed by relief. The urine never appeared cloudy except following an attack. At cystoscopic examination the left ureteral catheter entered for a distance of about 4 cm., and pus did not come from the stump on withdrawal of the catheter: this showed that there was no infection of the portion of the left ureter remaining after its incision at the time of hysterectomy. It was impossible to find the orifice of the transplanted ureter. The abdomen was opened, and many adhesions were found between the intestines and the abdominal wall; the omentum was adherent to the bladder at one point. All of the adhesions were freed, and on the upper left quadrant of the bladder the transplanted ureter was found extending across the pelvis for a distance of about 7.5 cm. At the point where the ureter left the pelvic wall below the brim of the pelvis, it was buried in dense scar tissue. The ureter was resected close to the bladder, and the remaining stump cauterized and inverted into the bladder. Due to the scar tissue, it was difficult to dissect the buried portion of the ureter. The remaining part of the ureter lying along the muscle bed was easily traced to its termination and resected. The part of the ureter resected was about 18.75 cm. long. It was contracted near its juncture with the bladder, where there was a portion of thin-walled dilatation. Within the cavity was thin purulent material which contained colon bacilli and staphylococci.

Stricture.—Campbell²⁶ stated that faulty drainage is the cause of infection of the urinary tract in infants as well as in adults. In 2,420 children coming to necropsy at Bellevue Hospital, ureteral blockage was found in 47 (approximately 2 per cent). Urinalysis or postmortem examination revealed infection in four fifths of these. In a large number of children with chronic pyuria, ureteral obstruction was found as the underlying lesion. Most of these acute renal infections ended favorably within two or three weeks, but there was a large group which resisted all forms of treatment.

Campbell reported a series of seventy-four cases of ureteral obstruction in infancy and early childhood. He used the classification of intra-ureteral or extra-ureteral, since these characteristics determine to a large degree the type of surgical procedure. The chief obstructions of and within the ureter itself were found to be strictures, including the formation of valves, calculi, kinks and anomalous conditions. Strictures, whether congenital or acquired, were the predominating ureteral obstructions in infancy. Congenital strictures were not infrequent and occurred at the two ends of the ureter, the ureteropelvic or uretero-

²⁶ Campbell, M. F.: Ureteral Obstruction in Infancy, *Am. J. Surg.* 5:445, 1928.

vesical junctures. In twenty-two patients, the blockage was bilateral; this condition was found in one instance in a 7 months' fetus. Campbell expressed the belief that the formation of stone is favored by urinary stasis and is most often associated with obstruction. Obstruction by acute ureteral angulations was associated with nephroptosis and renal ectopia, usually occurring at or near the ureteropelvic juncture. This type of blockage was characterized by marked hydronephrosis above and a relatively normal ureter. In cases of complete reduplication, obstruction rarely occurred at the point the ureter crossed in the pelvic cavity just above the bladder. Abnormal ureteral insertion may be found high in the renal pelvis with marked angulation or a lip valve which obstructs drainage. There may be ectopic insertion into the bladder, urethra, vagina or rectum.

Extra-ureteral masses were found to be predominantly inflammatory or neoplastic. Aberrant vessels usually passed from the lower renal pole to the aorta or vena cava. Chronic pyuria and pain in the loins were the usual symptoms.

The chief symptoms were hematuria, urinary frequency, dysuria, ureteral colic or dull aching in the loins with or without radiation. Chronic pyuria was the most constant symptom. In some cases palpation may reveal a renal mass, varying markedly in size. The onset may be acute and often follows an acute focal infection, but the urinary infection does not clear up within the usual time. In some cases pyuria was noted from birth, and in a few congenital ureteral obstruction with associated infection was noted at necropsy. The degree of obstruction is largely reflected by the temperature and pyuria.

Obstructive urinary lesions are characterized by dilatation, infection and renal destruction. Dilatation was usually more marked above the point of obstruction, but the inflammatory type was not infrequently observed below this point.

Relief of obstruction is the object of treatment. Dilatation of ureteral strictures afforded marked clinical improvement but bacteriologic cure was obtained in only three of Campbell's cases. He stated the belief that clinical improvement resulted from dilatation rather than lavage. Water in abundance is prescribed as the best medicine, and alkalis are of value when they promote diuresis. Medical measures are of value only when used with surgical procedures to relieve the obstruction. Early recognition and treatment save extensive renal destruction and often years of suffering or early death.

BLADDER

Tumors.—Hunt²⁷ stated that difficulty in evaluating reported results in favor of various methods of treating malignant tumors of the bladder

27. Hunt, V. C.: *The Surgical Treatment of Malignant Tumors of the Bladder*, J. A. M. A. **91**:1704 (Dec. 1) 1928.

is due to the lack of uniformity in classifying them according to the type of lesion, the degree of malignancy, and the situation and extent of involvement.

He found epithelioma, with varying degree of malignancy, in 95 per cent of the cases. Regardless of the site of the lesion, in a series of 480 epitheliomas graded on a scale of 1 to 4, 10 per cent were graded 1 (least malignant), 32 per cent were graded 2, 35 per cent were graded 3, and 23 per cent were graded 4, making a total of 58 per cent of a high degree of malignancy. The epitheliomas of the base of the bladder tend to be more highly malignant than those of the lateral wall or the dome. If all other conditions are equal, 10 per cent better results may be expected in the treatment for epitheliomas of the lateral walls and dome, simply because of the degree of malignancy.

The time of beginning treatment was found to have a significant bearing on operability and on the results of treatment. In a series of fifty-one cases in which the condition was too far advanced for any form of treatment, it was found that the average duration of symptoms previous to medical treatment was almost two years. Bumpus reviewed a series of 212 cases in which radium alone, or radium in conjunction with some other forms of treatment, was employed. He concluded that the use of radium alone is not successful in cases in which other methods of treatment cannot be used, that poor results are obtained when radium treatment is followed by operation, and that radium is most useful in connection with fulguration or operation. Hunt considered cautery excision as the method of choice for tumors of the lateral and posterior walls and dome of the bladder. Recurrence at the primary site of the lesion is less likely to follow.

The mortality rate of surgical procedures depends on the site of the tumor, the magnitude of the operation and, in lesions of the base of the bladder, on the method of disposing of the ureter. The mortality is lowest following the excision types of operation employed in the lateral walls and dome, and highest in segmental resection for tumors of the base with reimplantation of the ureter. Division and ligation of the ureter has proved the best method if the ureter is involved in the lesion or in extensive operable tumors of the base. In approximately 370 cases of epithelioma of the bladder, the results were dependent on the site of the tumor, the extent of the involvement and the degree of malignancy. In general, about 65 per cent of the patients with lesions graded 1 or 2 are living and well three years after operation, while 35 per cent of those on whom the radical operation was performed for lesions graded 3 or 4 showed equally good results. Approximately 73 per cent of the patients having tumors of the lateral walls or dome graded 1 or 2 and 42 per cent having tumors graded 3 or 4 are living three or more years afterward; 50 per cent of those having lesions

in the base graded 1 or 2 and 25 per cent having lesions graded 3 or 4 lived without recurrence for the same period.

Aschner²⁸ stated that several factors are responsible for the fact that vesical neoplasms are regarded as different from tumors elsewhere in the body and not subject to the usual mode of classification. There is a tendency for benign papillomas to implant themselves in other parts of the bladder and in the suprapubic wound after open operation, and also for new tumors to develop after the original tumor has been destroyed. Patients with papillomatosis or those who have been cured of papilloma may later have frank carcinoma of the bladder or metastatic phenomena with a malignant clinical course, and rare cases of papilloma with typical benign cell structure may show infiltration of the wall of the bladder.

The ordinary variety of papilloma is a soft, shaggy, villous tumor arising from the mucosa of the bladder by a well defined pedicle. The skeleton is formed by a delicate connective tissue core continuous with the submucosa of the bladder and containing blood vessels. The non-infiltrating type of papillary carcinoma may be pedunculated or sessile. It is usually indistinguishable cystoscopically or grossly from benign papilloma, from which a large percentage probably develop. The cell changes which indicate a malignant condition may be slight and limited to a small part of the growth, or marked and present throughout the growth. Nonpapillary carcinomas are characterized by their tendency to spread downward into the wall of the bladder and laterally under the normal mucosa, and often by ulceration and necrosis at the center of the growth. They seem to arise from the deeper cells of the mucosa, nests of which are not infrequently seen dipping downward in inflammatory processes, especially at the trigone and vesical neck.

Aschner concluded that in 97 per cent of the cases cystoscopic biopsy furnished the most reliable information as to the nature of tumors of the bladder. The failures occurred in multiple tumors and in papillomatosis. Prognosis cannot be made from biopsy alone in cases of malignant disease. The use of radium or operation, except on a debilitated patient, is indicated when a diagnosis of malignant disease is made in a case simulating papilloma. Aschner stated the belief that tumors of the bladder are benign or malignant, and that they may be classified in a manner harmonious with general tumor and clinical terminology. He did not consider cell grading alone as practicable for clinical purposes, and prognosis on such a basis does not coincide with the late results in his series of cases. Infiltration appears to be a more reliable guide to the extent of the lesion, and the site of the malignant tumor determines its resectability and influences prognosis materially.

28. Aschner, P. W.: *The Pathology of Vesical Neoplasms: Its Evaluation in Diagnosis and Prognosis*, J. A. M. A. **91**:1697 (Dec. 1) 1928.

The surgical procedure of choice when a diagnosis of carcinoma is made by biopsy is resection of the whole thickness of the wall of the bladder. Failure to do so, even in the case of pedunculated tumors, has often resulted in recurrence. Stalk invasion and tumor cells in blood vessels at the base cannot be detected by gross inspection. Only 20 of 137 papillary carcinomas were not infiltrating. Aschner expressed the belief that biopsy should always be made before radical operation on the bladder is undertaken, as other lesions may closely resemble neoplasm.

Stone.—Cabot²⁹ classified the cases of complicated stone in the bladder as cases in which the bladder is the seat of some other condition requiring surgical treatment. One of his fundamental principles when studying a patient with stone in the bladder is to determine whether there exists in the bladder some condition other than lithiasis which requires surgical treatment. If there is obstruction, diverticulum or other abnormality, the treatment for the stone becomes secondary to that for the other lesion.

Stone in the bladder may be treated by incision or by crushing and evacuation by instruments. Litholapaxy is the method of choice when it can be carried out satisfactorily. Indian surgeons are unanimously in favor of litholapaxy because convalescence is shortened, shock is lessened, and suprapubic scars are avoided. Cabot stated that there are several contraindications to litholapaxy. It should not be performed when there is disproportion between the size of the stone and the capacity of the bladder. When a large stone lies in a more or less contracted bladder, the movements of the instrument are limited; the amount of trauma resulting from many fragments is considerable and the time consumed in the operation, even if it is successful, is of disadvantage to the patient. In general a bladder that holds less than 125 cc. and contains a stone of considerable size will not be suitable for litholapaxy. Great surgical skill and experience may definitely modify this statement. Cabot considered the second contraindication to be cases in which the stone has as its nucleus a metallic foreign body or other substance which cannot be crushed. Before the development of the roentgen rays, it was difficult to determine with certainty the nature of the foreign body previous to operation. Litholapaxy should not be performed if the necessary instruments cannot be passed through the urethra. Stricture of the urethra is not a contraindication, since it can be readily divided by internal urethrotomy.

The group of borderline cases includes some of those in which the stone has a foreign body as its nucleus and a group in which the stone

²⁹ Cabot, Hugh: The Principles of Treatment of Stone in the Bladder. J. A. M. A. 91:1958 (Dec. 22) 1928.

lies not in the bladder but in a more or less dilated prostatic urethra. Some of the latter group may be considered as possibly satisfactory subjects for litholapaxy.

Diverticula.—Lower and Higgins,³⁰ from a study of the literature and their own experience, noted that the walls of diverticula vary in thickness, generally increasing with progressive inflammation of the diverticulum, although there may be a variation in different portions of the same diverticulum. The most common site of diverticula is proximal to one of the ureters, but no region of the bladder is exempt. Durrieux found records of fifteen diverticula situated in the trigone. Because of the quantity of fluid they contain, large diverticula tend to force their way backward, generally along the line of least resistance. Small diverticula usually lie between the bladder and rectum and, as they increase in size, extend laterally and upward. As a rule the orifice is quite small and entirely out of proportion to the size of the sac. The difficulty in emptying this type of diverticula makes them resistant to palliative treatment. The ureter may open directly into the diverticulum or may be incorporated in the wall of the diverticulum itself.

Diverticula are relatively infrequent in women. Rose's explanation of this is that in the female bladder, due to the absence of prostatic and seminal vesicle fixation, there is less loss of elasticity and less opportunity for diverticula to develop. Rathbun holds that all true diverticula are congenital and that the so-called acquired diverticula are only "exaggerated trabeculations." Diverticula may occur at any age, but they usually occur after the age of 50, during the period of prostatic obstruction.

The most common complications of diverticula are infection, calculi and tumors. Stagnation and infection are naturally conducive to the formation of stones, and these factors are usually present in varying degrees in such cases. Calculi in the diverticulum may be single or multiple. If they are multiple they may become faceted and lie close together, so that only the roentgen rays will show that more than one stone is present. When large stones are found in the diverticulum, they are usually associated with lithiasis in the bladder.

Diverticula do not cause definite symptoms, and the clinical picture varies with the presence or absence of infection. Many diverticula are discovered in cystoscopic examination in cases in which their presence has not been suspected, especially in hypertrophy of the prostate gland. The following diagnostic technic is used: Cystograms are made under the fluoroscope. After the bladder has been catheterized and drained, it is refilled with a solution of sodium iodide. A solution of from 10 to

30. Lower, W. E., and Higgins, C. C.: *Diverticula of the Urinary Bladder with Report of One Hundred and Ten Cases*, J. Urol. **20**:635, 1928.

17 per cent may be used without apparent irritation of the bladder. As the bladder is gradually filled, a close watch is kept for the appearance of irregularities which might be caused by hypertrophy of the prostate, tumors of the bladder, trabeculations or diverticula.

The present trend of treatment for diverticula is toward radical excision of the entire sac. As diverticula are usually associated with obstruction, the cause of the latter must also be removed in order to secure a satisfactory end-result. Lower operates under spinal or sacral anesthesia; in the case of an apprehensive patient, he adds analgesia with nitrous oxide and oxygen. A median suprapubic incision is made and carried down to the bladder. After the peritoneum is stripped back, the bladder is opened. Exposure of the interior of the bladder is secured with flexible retractors and a Cameron light. The diverticulum is located, and from its size and position the mode of procedure is determined. If the extravesical approach is used, the collapsed diverticulum is first converted into a solid or semisolid tumor by packing it with a gauze tape. Lower then dissects down outside the bladder, severing the attachment of the diverticulum and closing the opening into the bladder. It is important that the closure of the bladder at the point of removal of the diverticulum be made with good muscular apposition, the walls being inverted if possible so as to leave a slight ridge on the inner surface of the bladder rather than a depression at the point from which the attachment of the diverticulum was removed. Such a depression might serve as a starting point for recurrence of the diverticulum.

In forty-five cases of the series, the diverticulum was excised. There were three operative deaths (7 per cent). Twelve of the patients have not been traced since operation. Five patients have died since operation. Of the remaining twenty-one patients, observed for periods varying from six months to fourteen years, the average postoperative period was four years; marked improvement was noted in twelve; in nine, there was complete relief of symptoms.

Prognosis is usually favorable if radical operation is performed early and before renal impairment has become marked. In cases in which a malignant growth is present, the prognosis must be guarded.

Fistula.—Farman and Thompson,³¹ before attempting an operation for a vesicovaginal fistula, follow the principle of correcting any cystitis or other intravesical complication. Such a procedure presupposes a thorough cystoscopic examination of the bladder, determination of the exact size and situation of the fistula, and its relationship to the ureters. Small fistulas involving the lower part of the vesicovaginal septum

31. Farman, Franklin; and Thompson, R. C.: *Vesicovaginal Fistula: Etiology, Surgical Principles of Repair and Technique of Suprapubic Transvesical Operation*. J. Urol. 20:663, 1928.

usually are more readily accessible and lend themselves better to proper dissection and closure by the vaginal operation or one of its modifications. Fistulas high in the vagina are difficult to close, and failure is frequent by the vaginal route.

In repairing vesicovaginal fistula, a proper exposure of the operative field is made, as success depends on accurate and complete closure with well placed sutures in healthy tissue. All scar tissue is dissected from the thick vesicovaginal septum until the denuded, raw surfaces are soft and plastic. This will usually leave an opening two or three times the size of the original fistula to be closed by suture. Mobilization of the bladder is one of the most significant steps in the technic of repair; it permits the viscus to return to a more normal position (retraction upward and forward), and tends to separate the opening in the bladder from the opening in the vagina. It is necessary to secure a tight non-leaking closure that is urine proof. The method of suturing should be adapted to the size of the openings, elasticity of the tissues and accessibility. Circular, purse-string, lockstitch or continuous through-and-through sutures may be used. Chromic catgut generally is required for the main sutures. Opinion varies as to the necessity, method and length of time advisable for drainage of the bladder during healing. The majority of surgeons using the vaginal route for repair have drained the bladder after from six to ten days with a Pezzer catheter. A few have performed suprapubic cystostomy. The idea of drainage by catheter or cystostomy is to immobilize, during healing, the previously mobilized floor of the bladder and to relieve pressure on the line of suture.

The success of operation depends partially on skilled postoperative care, for any complication may be the undoing of the repaired fistula. Infection of the part usually means failure, but it is well known that tissues in this region possess a high degree of healing properties and local resistance. It is important to prevent spasm of the bladder, unnecessary movement or straining, restlessness, constipation, and contamination of the pelvic parts. Mayo and Walters expressed the belief that the success of repair depends on healing in the line of suture and accurate closure of the openings in the bladder and vagina. Some operators suture the openings at right angles to each other.

Paralysis.—Cahill³² observed that in conditions causing paralysis or destruction of the spinal cord, retention of urine began at once and continued until the bladder was greatly distended and showed in the lower part of the abdomen as a large ovoid tumor. The bladder still retains the power of contraction and should be properly stimulated so that it will gradually assume the power automatically to relieve itself.

32. Cahill, G. F.: Treatment of Bladder Paralysis Due to Non-Tabetic Spinal Cord Lesions, *Am. J. Surg.* 5:442, 1928.

In treating patients with paralysis of the cord with resulting urinary retention, Cahill does not perform catheterization but allows the bladder to fill for twenty-four hours and then forces the relief of the bladder by pressure excited on the fundus. When the bladder can be clearly and easily felt, the right or left hand is placed sidewise across the fundus and the ulnar side pushed above the fundus as far as possible into the abdomen. The fundus is then cupped or grasped and pressure exerted by pushing down against the pelvic opening. The urine may not appear for one or two minutes after pressure and then may be voided only in a small irregular stream. Pressure is then applied every two hours, each time the amount of urine obtained slowly increasing and the pressure required decreasing. It usually takes from six to ten days before the bladder empties well behind the symphysis and several weeks before it empties completely. If possible, Cahill instructs patients how to apply the pressure themselves, and sometimes they are able to hasten the emptying of the bladder by applying their own increase of abdominal tension by breathing.

If there is infection, catheterization is instituted but only until the infection has subsided.

Cysts.—Altmann³³ stated that cysts of the posterior wall of the bladder, especially in the prostate gland, are comparatively uncommon. Eliminating echinococcus and dermoid cysts, Meyer considered the following as etiologic possibilities: (1) fetal inclusion of the prostatic utricle due to epithelial adhesions, that is, a sealing off of the terminal portion with a subsequent cystic dilatation of its lumen as well as a disturbance in the development of the mullerian duct; (2) cystic dilatation of the prostatic and trigonal glands; (3) abnormal persistence of portions of the mullerian duct derived from its terminal segment, and (4) offshoots from the seminal vesicles and ducts. On account of the frequent association of the cysts with the utricle, Altmann favored the first hypothesis. Hypotheses regarding the association of neighboring glandular structures may be assumed. The second group comes in this classification.

A case of a man, aged 19 years, is cited which could be classified in the third or fourth group. Necropsy revealed marked hydro-ureter and hydronephrosis on the left side, associated with the seminal vesicles and vas. A large piece of adjacent tissue and wall of the bladder was removed in order to study the case thoroughly. The inner wall of the cyst was composed of a double layer of cubical epithelial cells. The cyst was entirely closed off from adjacent tissues.

33. Altmann, Franz: Zur Kenntnis der Cysten an der hintern Blasewand beim Menne, *Ztschr. f. urol. Chir.* 24:438, 1928.

There are only nine reported cases in the literature, in all of which the cysts were small, about 2 cm. in size, and were found at varying ages, from birth to old age. Six were in the median line just above the prostate gland, and three were situated below the prostate gland and medially to the vas. Most of the cysts were oval or pear-shaped. Histologically, all cysts were lined with cubical epithelium. In two cases, including that of Altmann, muscle fibers were found in the wall of the cyst. This was interpreted as meaning an association with the ductus deferens.

Exstrophy.—Judd and Thompson³⁴ stated that the ultimate cause of exstrophy of the bladder is not known, but the existing theories collectively purpose that it results from mechanical rupture, pathologic lesions, or defective embryonic development. Histologic studies reveal that the structure of the bladder in cases of exstrophy is usually unlike that of the normal bladder, and glands have been constantly observed. There are usually varying degrees of local inflammation, the result of mechanical and chemical irritation and infection. Associated ascending infection is common, and death usually is caused by toxemia of infection or of renal insufficiency.

Judd and Thompson described 2 cases of carcinoma complicating exstrophy of the bladder, making a total of 20 reported cases. Adenocarcinoma was reported in 15 cases and squamous cell carcinoma in 2; a histologic report was not made in 3 cases. Although adenocarcinoma is of comparatively rare occurrence in the normal bladder, it is the type which most commonly occurs in exstrophy of the bladder. Nineteen (2.19 per cent) adenocarcinomas were found among 867 tumors of the normally developed bladder at the Mayo Clinic. Of the 20 reported cases, 12 occurred in men and 7 in women; in 1 case, the sex was not mentioned. Two occurred in the third decade, 5 in the fourth, 9 in the fifth, 3 in the sixth, 1 in the seventh. Surgical treatment was employed in 10 of the 20 cases. In 3, simple extirpation of the bladder was performed. In 1 case, transplantation of the ureters by the Mayo method preceded removal of the bladder. The patient died two years after operation from metastasis. In 2 cases cited by Judd and Thompson, the patients are alive and well three, and six and a half years respectively, after operation. In 3 other cases transplantation of the ureters into the colon was performed. One of the patients died eight days later from uremia following ascending renal infection. In the other 2 cases, resection of the bladder was performed secondarily.

Vesical Neck.—Herbst³⁵ observed that although the symptoms of fibrosis of the neck of the bladder may not be marked until adult life

34. Judd, E. S., and Thompson, H. L.: Exstrophy of the Bladder Complicated by Carcinoma, *Arch. Surg.* **17**:641 (Oct.) 1928.

35. Herbst, R. H.: Fibrosis of the Vesical Neck, *J. A. M. A.* **91**:1614 (Nov. 24) 1928.

or later, a surprisingly large number of these patients give a history of disturbances of the bladder in childhood.

The appearance of the bladder, as well as the symptoms of fibrosis, is quite different from that found in other obstructive conditions. Fibrosis of the vesical neck is generally characterized by a small contracted bladder with massive thickening and hypertrophy of the wall, instead of a large dilated bladder with moderate hypertrophy of the muscle coat. The symptoms of fibrosis may be classified as those referable to the bladder and those produced by changes in the upper urinary tract. The bladder is usually small and often contracted because of the hypertrophy of the muscular wall, a condition which frequently causes an active form of incontinence, in contrast to the passive overflow type seen in other forms of obstruction. Urgency and frequency of urination are prominent symptoms. Complete retention is infrequent due to the powerful contraction of the hypertrophic wall of the bladder, but regurgitation to the upper urinary tract is more pronounced than in most other types of obstruction. On rectal examination, the prostate gland is usually about normal in size and in consistence. If an instrument is introduced into the bladder, resistance may be encountered immediately at the neck of the bladder, which as a rule is easily overcome. In uncomplicated cases there is marked trabeculation, the trabeculae being heavy with deep cellules between them. The vertex of the bladder is more contracted than the lower part, causing the formation of a dome which at times may be mistaken for a diverticulum.

Herbst stated the belief that the degree of retention and the impairment of the renal function should be determined so as to distinguish between the cases of fibrosis in which the condition can be corrected without drainage and those in which drainage is required. He considered some type of drainage by catheter to be preferable to preliminary cystostomy because of the difficulty encountered later in obtaining good exposure of the neck of the bladder, which is essential to thorough removal of the fibrotic neck. Some form of transurethral or punch operation is the method of choice in the milder types of fibrosis, particularly those in which the lower segment of the internal urethral orifice is most involved.

Mucous Glands.—Edelman³⁶ reported two cases from Mount Sinai Hospital in which intestinal-like mucous glands were found in the urinary bladder. Both patients complained of frequency, dysuria and hematuria, suggestive of new growth or intense cystitis. One gave a history of having passed gravel.

³⁶ Edelman, Leo: Muciparous Glands in the Mucosa of the Urinary Bladder, *J Urol*, 20:211, 1928.

Some observers deny that mucous glands exist in the urinary bladder; others admit their presence; others interpret them as aberrant prostatic or urethral glands. The cases reported in the literature showing lesions containing "intestine-like" mucous glands have their origin ascribed to misplaced embryonal intestinal glands, to embryonal rests, to proliferation and metaplasia of the surface epithelium (Enderlen), to proliferation of lesions in cystitis cystica due to an inflammatory process (Stoerk and Zuckerkandl), and to proliferation of mucous glands normally present in the mucosa (Bridoux).

The lesions do not cause distinctive symptoms. The patients usually complain of frequency, dysuria and hematuria. Therefore, the diagnosis can be made only by microscopic examination of the tissues removed. The treatment is either excision or destruction with the cautery. The persistence of these glands may possibly be the basis for the development of adenoma or adenocarcinoma.

PROSTATE GLAND

Hypertrophy.—Davis³⁷ summarized the immediate and later results in a series of 176 consecutive cases in which perineal prostatectomy was performed under sacral anesthesia in an attempt to determine the immediate mortality and the percentage of satisfactory functional results. There were 3 deaths (1.7 per cent) in his series. The average age of the patients was 70; 16 were more than 80 years of age, two of these being 88.

Davis stated that the factors instrumental in reducing the mortality rate of prostatectomy are preliminary drainage, sacral anesthesia and careful hemostasis. Good hemostatic control is particularly important, as many deaths may result from hemorrhage due to infection secondary to lowered resistance. Prostatectomy may be made an almost bloodless procedure as the result of the opportunity for deliberateness in controlling individual bleeding points by suture and ligature which is afforded by the employment of sacral anesthesia, and the use of an inflated hemostatic bag to control hemorrhage during the first few postoperative hours. The anesthesia used in all of Davis' cases was sacral block, including injection through the sacral hiatus (caudal anesthesia), as well as through the first, second and third sacral foramina on either side. This type of anesthetic has eliminated the problem of anesthesia for prostatectomy in old and debilitated patients. It is easily and simply administered, is almost uniformly efficient, and does not cause complications. There was not a death nor a reaction of consequence in his entire series. Hemorrhage should be treated as an

37. Davis, Edwin: Perineal Prostatectomy Under Sacral Anesthesia, J. A. M. A. 91:1618 (Nov. 24) 1928.

emergency measure and should be checked by mechanical means, even though it necessitates a secondary operation.

Davis expressed the belief that functional results should be as significant, if not more so, than the immediate mortality rate. Good functional results are dependent on accuracy in preoperative diagnosis as well as on proper operative technic. On the basis of his late observations and on the assumption that there has been a proper diagnosis, preparation and operative technic, Davis made a conservative estimate that one may expect 80 per cent of satisfied patients following prostatectomy and 15 per cent of fairly satisfied patients.

Lewis³⁵ employed perineal prostatectomy exclusively for several years, but for the last fifteen years he has obtained better results with the suprapubic method. He pointed out that, even though Davis had a low immediate mortality rate in his series, in 36 of 100 patients traced the condition remained uncontrolled, while six cases of fistula resulted. He believed that these should not have been present in any of the cases in which prostatectomy was performed.

Thomas,³⁵ stated that the mortality rate of Davis will not be improved for a long time. He expressed the belief that Davis should not be permitted to convey the idea that in all cases of prostatic hypertrophy operation should be performed by the perineal route. If those who practice this method exclusively would give more attention to the route and make the type of operation dependent on the pathologic changes present, not only would the present mortality rates be lowered but improvement would attend the morbidity results. It is Thomas' belief that there is something wrong with urology when some of the leading exponents contend that prostatectomy should always be done suprapubically, while others insist that it should be done perineally.

Livermore³⁵ has favored the suprapubic method of prostatectomy because he has obtained better results and considers himself more skilled in it. It is his opinion that the choice of technic is a personal matter.

Foley³⁵ stated the belief that it is useless to attempt a comparative appraisal of perineal and suprapubic prostatectomy because of the prejudice of advocates of the two operations. He considers perineal prostatectomy a technically difficult procedure, the main difficulty being the proper division of the recto-urethralis muscle. If technical faults on the part of the operator are not considered, the perineal operation regularly gives a functional result as good as it is possible to obtain by the suprapubic approach. A poor functional result means an incorrect dissection. To him there is no latitude between the proper dissection which will give a perfect functional result and an improper one resulting in incontinence or injury to the rectum.

³⁵ In discussion on Davis (footnote 37).

Carcinoma.—Roberts³⁰ reported three cases of carcinoma of the prostate. In the first case he found metastasis to the skull, the left clavicle, the left fifth rib, and the abdominal lymph drainage limited to the pelvic vessels. The outstanding features of the second case were the involvement of the upper dorsal vertebrae and the fourth left rib, together with the absence of any involvement of the abdominal lymph vessels above the level of the second lumbar vertebra.

A study of these cases, together with others of a similar nature showing involvement of the skull and upper dorsal region, suggested the possibility of a constant path of dissemination from the primary growth in the prostate gland. On theoretical considerations the spinal canal was regarded as a possible route, and it was further indicated by the widespread involvement of the pelvic bones sometimes seen in these cases. It was therefore decided to examine the spinal column in all cases in the future. In Roberts' third case, necropsy serves to support the contention. At necropsy the spinal laminae, with the ligaments, were removed in one piece from the cervical to the lower lumbar region, and at once plaques of growth were seen to involve the whole length of the ligamenta subflava and the intraspinal surface of the laminae. Both the dura mater and its contents and the posterior common ligament appeared to be normal. There was an almost continuous direct spread of growth on the intraspinal surface of the dorsal wall of the spinal canal from the sacral to the cervical region, whereas the abdominal lymph spread had extended only as far as the upper lumbar region. It is interesting to note that the thoracic duct was uninvolved throughout its thoracic course. Histologic section of the temporal bone showed marked invasion by carcinoma cells of the same types as those found in the pelvic lymph glands and prostate gland. A section of the lamina in the upper dorsal region also showed columns of carcinoma cells in the spaces of the connective tissue of the ligaments and periosteum of the laminae; some of these columns appeared to be surrounded by a layer of endothelial cells suggesting lymph vessels, while others appeared to lie in close contact with the connective tissue fibers and cells. The spinous process and lamina were also extensively involved.

Roberts discussed the usual methods of the spread of metastasis and suggested that another route plays an important (and perhaps the most important) part in the distant dissemination of malignant cells from the prostate gland. This path consists of the lymphatic vessels and tissue spaces of the spinal laminae with their associated ligaments. Structurally, the ligamenta subflava consists of elastic tissue fibers with a network of lymph spaces both between and on the surface of the fibers

39. Roberts, O. W.: Some Notes on Carcinoma of the Prostate; Including Evidence of an Intraspinal Route of Dissemination, *Brit. J. Surg.* **15**:652, 1928.

of which they are composed; also, the interspinal ligaments have loose connective tissue between the fibrous framework. The path by which the cells reach the spinal canal is at present unknown, but in a recent postmortem examination two likely pathways were noted. One path is by the lymph drainage of the prostate gland to the sacral lymph glands; these glands lie near the anterior sacral foramina and, in this case, were found to be extensively invaded. It is possible that permeation of lymph vessels by the carcinomatous cells may obstruct the flow of lymph from the sacral glands to the iliac and para-aortic vessels and may lead to an increase of flow through the vessels linking up the intraspinal with the intra-abdominal lymph vessels. Along this path, the malignant cell would be able to grow and permeation or emboli occur readily. The other path noted was the loose connective tissue lying on the surface of the levator ani and coccygeus muscles; a tongue of new growth was found passing from the prostate gland toward the anterior sacral foramina in this tissue. Histologically, the growth appeared to be due to infiltration of loose tissue rather than to lymphatic permeation, but further sections are necessary before this question can be decided. The pelvic nerves appeared to be free from invasion, as did the blood vessels. By this intraspinal route, rapid dissemination to distant parts of the body is feasible. The vertebrae, ribs and skull are accessible to the invading cells, and the involvement of the bone-marrow of these bones may account for the extreme anemia and asthenia in cases in which metastasis is so widespread. Theoretically, one would expect changes in the lymph flow in the upper dorsal region, since the main lymph vessel and its branches in this region are subject to the suction action of the respiratory movements of the thorax and of the negative pressure in the great veins. In this way permeation of vessels in the upper dorsal region, especially of the left side, would be explained.

Wildbolz⁴⁰ operated on forty patients with carcinoma of the prostate. Three (7.5 per cent) of the patients died from the operation; thirteen (30.2 per cent) had either multiple metastasis or local recurrence from eighteen months to three years after operation; four died from one to three years after the operation of other diseases, without evidence of malignant recurrence; twelve lived more than three years after the operation, and were completely free of the trouble and without evidence of recurrence; these might be said to have had an operative cure. One patient died of pneumonia nine years after operation, two died of heart trouble six years after operation, and one died of apoplexy five years after operation. Five patients were completely well at the time this paper was written, more than three years after operation. In all of these cases, the diagnosis was made by histologic examination.

40. Wildbolz, Hans: Die Erfolge operativer Therapie des Prostatakarzinoms, Schweiz. med. Wchnschr. 58:726, 1928.

TESTES, EPIDIDYMIS AND SEMINAL VESICLES

Carcinoma.—Scholl⁴¹ reported the case of a man, aged 22, who came for relief of pain in the right inguinal region and because of swelling of the right testis, which had been severely injured while he was playing football fourteen months before. For six months there had been a gradual swelling of the right side of the scrotum, until it was about twice its normal size. The testis was smooth, rounded and slightly larger than normal. The epididymis could be identified easily; it was distinctly separate from the testis and markedly enlarged.

At operation the testis was not increased in size and apparently was not diseased; it was smooth, rounded and a normal bluish white. The epididymis was greatly enlarged and irregular in contour. It was readily separated by sharp dissection from the testis. There was no invasion of the testicular substance, which was normal in size, shape and consistence. The epididymis was nodular and reddish. The vas was separated and a short segment removed with the epididymis. Microscopic examination revealed the growth to be malignant and the testis, the surrounding coverings and the cord were removed. Three months after operation, a mass 2 cm. in diameter was found below the lower angle of the incision. At a second operation, the fascia of the external oblique muscle was opened and the stump of the cord excised at the internal ring. The cord, tumor and all the surrounding tissues, including the inguinal glands and subcutaneous tissue, were then removed. Enlarged inguinal glands were not found. The wound healed well, and the patient was given roentgen treatment over the lower portion of the abdomen and the area of recurrence.

Four months after the operation the patient became short of breath and cyanotic. Examination revealed a large amount of fluid in the right side of the chest. A needle was inserted into the base of the left pleural sac, and 4 liters of blood-stained fluid was withdrawn. Roentgen examination of the chest after removal of the fluid revealed a mass about 6 cm. in diameter in the region of the hilum of the lung. One week later a second tapping was done, and 2 liters of fluid was removed. After that the patient's chest was tapped about once every ten days, from 2 to 3 liters of fluid being removed at each tapping. The pathologist's diagnosis was adenocarcinoma of the epididymis.

Tuberculosis.—Young⁴² presented an analysis of twenty-two cases of genital tuberculosis in which he operated at least five years ago. In six cases nephrectomy was carried out in addition to the radical removal

41. Scholl, A. J.: Primary Adenocarcinoma of the Epididymis: Report of a Case, *J. A. M. A.* **91**:560 (Aug. 25) 1928.

42. Young, H. H.: Brief Note on Ultimate Results of Radical Operation for Tuberculosis of the Seminal Tract, *J. Urol.* **19**:679, 1928.

of the seminal tract. In several of these cases, severe urinary symptoms with involvement of the seminal vesicles and epididymis had developed in the tuberculous process. In most of the cases the condition of the patient was poor, with local involvement extending to the seminal vesicles and the prostate gland, as well as to the epididymis on one or both sides and sometimes to the testes. In five of the early cases only one seminal vesicle and one lobe of the prostate gland were removed, along with one side of the epididymis and one vas. Recurrence of tuberculosis in the remaining side of the epididymis has led Young to practice bilateral vesiculectomy and ampullectomy in cases of this type, with markedly improved results in eliminating subsequent involvement of the remaining epididymis. The prostate gland was involved close to the urethra in most of the cases. In four patients a persistent urinary fistula was present, leakage occurring only during urination, indicating that it came from the prostatic urethra and not the bladder. Patients were greatly relieved of pain, frequency of urination and hematuria by the operation of removal of the tuberculous seminal tract, even when pulmonary tuberculosis was present and was the cause of death. In five of six cases in which both vesiculectomy and nephrectomy were done, pulmonary lesions were present but at the last report only one patient had died.

In regard to operative technic, Young has found the use of caudal anesthesia usually successful in securing a painless procedure until the deep portions of the seminal vesicles and vas are attacked, and then local infiltration anesthesia is usually satisfactory in relieving pain.

There were no operative deaths. Six deaths are known to have occurred during the five years or more since operation: all of these patients had pronounced pulmonary involvement before operation. Fourteen patients (67 per cent) have been traced and found in good condition from one to twelve years after operation (nine, more than five years; one, four years; three, three years and one, one year). Statistics show that seminal vesicles are involved in most cases of genital tuberculosis.

Barney and Colby⁴³ stated that genital tuberculosis takes its origin from either coexistent or healed extragenital lesions, which are usually found in cases of genital tuberculosis. In a large percentage of cases in which the epididymis is involved, clinical examination shows involvement of the prostate gland and seminal vesicles. There are two views as to the incipency of this disease: that it is primary in the epididymis, and that it is primary in the seminal vesicles. The bacillus of tuberculosis may be transmitted from the epididymis to the seminal vesicle

43. Barney, J. D., and Colby, F. H.: *The Treatment of Genital Tuberculosis in the Male*, J. Urol. 19:657, 1928.

with the stream of secretion, known as the "descending route," or the infection may follow the blood stream or "ascending route." Most writers favor the former route.

The lesions of the epididymis usually begin in the globus minor, and the seminal vesicle on the same side is the one usually involved. Possibility of involvement of the second epididymis is decreased by removal on the side first affected, and the excision of the vas on the apparently healthy side aids in curtailing the spread of the disease to that side. The testis may not become affected even after years of contact with a tuberculous epididymis.

Treatment may be surgical or medical. Radical operation involves the removal of the seminal vesicles, prostate, vas and epididymis, together with the testis if it is involved. Medical treatment may include minor operations but consists primarily of the administration of tuberculin, heliotherapy, roentgen rays and ultraviolet rays and does nothing more than arrest the progress of the disease in some instances, often without improving the general condition of the patient.

In the author's experience, epididymectomy resulted in as low an operative mortality and good results in general as the more radical operations. It has been frequently observed that following epididymectomy the disease found before operation in the seminal vesicles and prostate gland not only ceases to progress but actually retrogresses to the point of clinical cure. This observation gives support to the belief that the disease begins in the epididymis.

Many patients with genital tuberculosis eventually die of tuberculosis of the lung or of miliary tuberculosis, which is probably attributable to the original lesion in the lungs or bronchial lymph glands rather than to areas of disease which conservative operation or medical treatment has left behind.

Wildbolz⁴⁴ stated that acute tuberculous epididymitis is much more significant than is generally believed. In about 25 per cent of all the patients with tuberculous epididymitis that he saw the condition began with an acute period similar to that caused by infection with gonococci, colon bacilli or staphylococci. This acute onset occasionally leads to a false sense of security, and valuable time is lost. In order not to make serious mistakes, it is necessary always to remember that tuberculosis may produce acute epididymitis.

It is usually easy to distinguish acute tuberculous epididymitis from gonorrheal or other epididymitis. Acute tuberculous epididymitis is produced only in the presence of high allergy. This high allergy is only found if the patient has, at the moment, a virulent tuberculous infection,

44. Wildbolz, Hans: Nonspecific Chronic Epididymitis and Tuberculous Epididymitis, *Proc. Staff. Meet. Mayo Clinic* 3:169, 1928.

so that in most cases of acute tuberculous epididymitis tuberculosis of the bladder, kidney, prostate, seminal vesicles, lungs or joints will be associated. If the diagnosis does not seem clear, one must observe the patient a short time. In the case of gonorrheal infection or other infection, the infiltration of the epididymis will regress after a few days. In a case of acute tuberculous epididymitis diminution of the symptoms of acute inflammation will be noted, but the infiltration will not regress and will perhaps progress. This slow regression of infiltration must always be a warning that the epididymitis may be tuberculous.

In about 25 per cent of the cases the tuberculous infection is primary in the epididymis, and the epididymis should be removed. In more than 150 cases of epididymectomy which Wildbolz could trace for many years, there was no recurrence of tuberculosis of the testis when it was not present in the testis at operation. Wildbolz expressed the belief that the best way of preventing tuberculosis of the testis is removal of a tuberculous epididymis as soon as possible, and he does this even in the acute period of the infection. It is slightly more difficult to remove the epididymis in the acute stages, but the acutely inflamed epididymis can be detached and removed separately. As soon as it has been determined that the epididymis is tuberculous, either chronically or acutely infected, it should be removed at once. In 90 per cent of the cases, there will never be further passage of spermatozoa. Consequently, there is no reason for not removing it.

Wildbolz has tried the various conservative methods of treatment, such as tuberculin, roentgen rays and heliotherapy. Even after employing conservative nonsurgical methods for one or two years, he was not certain that the recovery was complete. He has removed the epididymis following treatment by conservative methods for from three to seven years, and has found many tubercles and virulent bacilli. He believes that in the reports of healing in cases of tuberculous epididymitis after roentgen or tuberculin treatment in a few weeks or months the condition was not tuberculous epididymitis but chronic nontuberculous epididymitis, a disease not yet universally known.

Seminal Vesiculitis.—Wassiljeff⁴⁵ stated that most of the literature deals only with the clinical diseases of the seminal vesicles and little with their pathologic anatomy. The seminal vesicles are often mentioned in association with various disease processes. Using the material from 120 necropsies, Wassiljeff attempted to determine the frequency of vesicle changes due to disease and age.

The collected material was divided into the following groups: six cases of syphilis (syphilitic mesa-ortitis with aneurysm and progressive

45. Wassiljeff, A. A.: Ueber die pathologischen Veränderungen der Samenblasen (auf Grund des Leichmaterials), Ztschr. f. urol. Chir. 24:502, 1928.

paralysis); ten cases of nonspecific diseases of the vascular system, arteriosclerotic and contracted kidney, and arteriosclerosis of the cerebral arteries; thirty-one cases of all types of tuberculosis, that is, of the lungs, kidneys, genital organs—acute, miliary and chronic; thirty-six cases of all types of acute and chronic septic processes, such as endocarditis and peritonitis, and also the acute infectious diseases; twenty-six cases of malignant growths of the various organs, and eleven cases of miscellaneous growths and diseases.

Changes in the seminal vesicles were grouped as follows: comparatively pure types of changes in the seminal vesicles due to age; changes which are on the borderline between those due to age and those due to pathologic conditions, and pure pathologic changes.

Wassiljeff stated that changes of the seminal vesicles due to age show themselves in thickening of the septums of the vesicles, in diminution of their lumen, in substitution of the muscle fibers by connective tissue, in deposition of pigment in the epithelial cells, and in complete atrophy of the vesicles. The vascular system of the seminal vesicle capsule is early affected with arteriosclerotic changes. Deposition of pigment in the cell elements of the walls of the vesicles and the formation of cystlike diverticula may also be attributed to changes due to age and is apparently aided by the cachectic diseases. The formation of cysts is probably instituted by inflammatory processes, increasing with the addition of connective tissue, and occasionally there may be obliteration of the lumen of the vesicle. Inflammatory processes were frequently found in the seminal vesicles, such as metastatic pus vesiculitis, chronic and acute catarrhal vesiculitis, chronic fibrous vesiculitis (dilated or atrophic vesicles) and chronic perivesiculitis.

Chronic inflammation of the vesicles was demonstrated in 47 per cent of the septic cases, in 80 per cent of the syphilitic cases, and in 19 per cent of the tuberculous cases. Tuberculous changes of the vesicles were found in 22.8 per cent of the cases of general tuberculosis. The calcification of the contents of the seminal vesicles results occasionally in cases of tuberculosis. In cases of malignant growths of the prostate gland and the bladder, infiltration of the walls of the seminal vesicles was observed. Metastasis from tumors of distant organs is not infrequently found but is usually overlooked, since macroscopic changes are not sharply outlined.

URETHRA

Carcinoma.—Robb,⁴⁶ in reviewing the literature, found that the lesion usually occurs deep in the bulbous urethra where it may arise

46. Robb, J. J.: Cancer of the Male Urethra: Report of Two Cases with a Short Survey of the Subject, *Brit. J. Surg.* **15**:605, 1928.

from Cowper's glands or from other glandular structure. The case reported by Robb is apparently the first one on record in which cancer of the urethra originated in a stricture. The patient, a man, aged 59, contracted gonorrhea at the age of 21. For six years he was treated for a stricture which had been dilated on 111 occasions, a total of 477 instruments having been passed. Eventually, it became impossible to pass instruments, and he was admitted to the hospital. A hard stricture could be felt at the penoscrotal angle, with a nodule about the size of a "small marble" on its upper and left side. The stricture was excised, and microscopic examination of the tissue revealed a transitional cell carcinoma. Further operation was refused at the time, but two and a half months later, on recurrence of the nodule, the patient consented to amputation. A case was reported also of a man, aged 69, who was admitted to the hospital with a suprapubic fistula following cystotomy. There was a dense mass in the perineum. A specimen removed revealed transitional cell carcinoma.

From seventy-six case reports from the literature in which evidence as to the nature of the tumor was available, the following list was compiled: squamous cell carcinoma, 73 per cent; columnar cell carcinoma, 1.5 per cent; papillary carcinoma, 3.5 per cent; adenocarcinoma, 21.2 per cent (from Cowper's glands), and transitional cell carcinoma, 1.3 per cent.

Great difficulty was experienced in determining the site of these tumors, owing to the insufficient data in the recorded cases. Robb, therefore, referred only to the sixty-one case reports found by Diehle and classified as follows: membranous urethra, thirty-three; pars cavernosa, twenty-six; and fossa navicularis, two. Recognition of the high percentage of squamous cell carcinomas which occur in the male urethra casts doubt on the small number originating in the fossa navicularis. Descriptions are inadequate to make this opinion decisive, but in a large proportion of cases in which the anterior part of the pars cavernosa is involved, the condition may originate in and around the fossa navicularis and thence spread backward.

Carcinoma of the urethra is rarely diagnosed in its early stages; most of the patients are treated for strictures of the urethra, and not until late in the course is the proper label affixed and adequate treatment begun. Robb expressed the belief that it would be true wisdom immediately to suspect every pathologic change toward the formation of tumor in the urethra as tending toward malignant disease and to treat it as such.

The symptoms of the disease may be divided into three stages. In the first stage, as in stricture, there is difficulty in urination because of the early obstruction by the tumor, a difficulty that is usually accompanied by urethral pain. Often there is a purulent or blood-stained

discharge. Retention of urine sooner or later occurs, and the picture immediately suggests simple stricture. The patient looks well but as a rule feels weak. This stage may exist for several months. In the second stage, a local tumor forms. In the third stage, infection is the predominating factor; periurethral abscess forms which, on bursting, results in fistula. In 80 per cent of the cases this fistula opens on the under surface of the penis.

Peters⁴⁷ stated that primary carcinoma of the male urethra is rarely encountered; there are less than 100 cases reported in the literature. Gonorrhea, stricture, leukoplakia or any other chronic inflammatory process is probably not of primary importance.

A case is reported of a patient, aged 42. The bladder was distended, and attempted catheterization met obstruction in the deep urethra. On incision, pus and urine were encountered in the tissues. The inflammatory portion seemed to be on the edges of a distinct mass of hard tissue which had not broken down, and sections taken for examination revealed epidermoid carcinoma.

Chute, in discussing Peters' paper, reported a case in which he made an opening into the urethra and curetted a cavity behind a urethral stricture. Fifteen years later, a mass in the left side of the perineum and a fistula near the penoscrotal angle were found. Some time later, Chute operated and removed a mass of hard tissue and a considerable portion of the left side of the urethra. Microscopic examination revealed carcinoma. A year later the patient returned, showing an area of recurrence entirely surrounding the urethra. Chute cut out a section of the urethra and sewed the ends together.

[COMPILER'S NOTE: Primary tumor of the urethra is extremely rare. In one series of 16,637 cases of tumors of various organs cited by Englisch,⁴⁸ no instance of malignant growth of the urethra was noted. In another series of 4,000 cases of disease of the male urinary organs, only 3 were of carcinoma of the urethra. In 358 cases of carcinoma of traumatic origin reviewed by Lowenthal,⁴⁹ there were 2 of carcinoma of the urethra.

Occasionally urethral carcinomas are preceded, as in Chute's case, by periods of urinary difficulty and irritation. The formation of tumor is somewhat analogous to the long-standing premalignant stages preceding the development of squamous cell tumors of the urinary bladder.

47. Peters, C. N.: Primary Epidermoid Carcinoma of the Male Urethra, *New England J. Med.* **199**:269, 1928.

48. Englisch, J.: Das Epithelium der männlichen Harnröhre, *Folia urolog.* **1**:38, 1907.

49. Lowenthal, Carl: Ueber die traumatische Entstehung der Geschwülste, *Arch. f. klin. Chir.* **49**:1 and 267, 1895.

König⁵⁰ reported a case of urethral carcinoma developing after urinary obstruction of forty-eight years' duration, and Oberlander⁵¹ noted a somewhat similar case developing after forty years of urinary difficulty.

The onset may be quite rapid in young persons. Barney⁵² and Fuller⁵³ both reported cases of sudden onset with acute retention. Schustler⁵⁴ reported a case of acute retention with fourteen days of uremia, followed by death. Most of these tumors occur at the usual site of the formation of the stricture. Of forty-two cases of carcinoma of the male urethra noted by Preiswerk,⁵⁵ thirty-eight were in the membranous or cavernous urethra.

Most of these carcinomas have a histologic structure similar to that of squamous cell epithelioma of the penis, although of a higher degree of malignancy. Metastatic growths, which are not common, have the same tendency to remain localized in the primary glands as do those arising from epitheliomas of the penis. At times the only symptoms are those resulting from moderate obstruction, together with marked hematuria, especially after urethral manipulation.

Diverticula.—Mouat⁵⁶ stated that urethral diverticula may be congenital or they may be acquired. Those in the prostatic urethra are most commonly acquired from the gradual increase in size and communication with the urethra of a sac containing prostatic calculi. In a less common type, the prostatic urethra may gradually become distended to form a sac as a result of the lodgment of stones in that portion of the canal. Mouat reported a number of interesting cases. In one a 2 ounce (56.7 Gm.) stone was found in a sac which communicated with the posterior urethra. At operation, the stone was cut down on from the perineum. It was deeply grooved on the surface, corresponding to the gap in the floor of the urethra. The pouch was excised, and the edges of the urethral opening were stitched together over a catheter inserted into the bladder.

In the anterior urethra, the acquired type of diverticula is much more common than the congenital variety. A case is described of a stone

50. König: Cancroid des Bulbus und der Pars nuda urethrae, Monatsbl. f. Urol. 6:641, 1901.

51. Oberlander, F. M.: Beitrag zur Lehre vom primären carcinoma urethrae, Internat. Centralbl. f. d. Physiol. u. Path. d. Harn. u. Sex-Org. 4:244, 1893.

52. Barney, J. D.: Cancer of the Male Urethra: Report of Two Cases, Boston M. & S. J. 157:790, 1907.

53. Fuller, E.: Six Successful and Successive Cases of Prostatectomy, J. Cutan. & Genito-Urin. Dis. 13:229, 1895.

54. Schustler, M.: Ueber einen Fall von Epithelil carcinoma in der Continuität der männlichen Harnrohre, Wien. med. Wchnschr. 31:157, 1881.

55. Preiswerk, P.: Ueber das primäre Karzinom der männlichen Urethra, Ztschr. f. Urol. 1:273, 1907.

56. Mouat, T. B.: Urethral Diverticula, Brit. J. Surg. 16:51, 1928.

in a pouch which communicated with the floor of the urethra at the penoscrotal juncture. The stone was cut down on, under local anesthesia, and removed from the thin-walled sac, which was tightly stretched over it. A small opening which communicated with the urethra was stitched up, and the thin-walled sac was obliterated.

In forty cases of acquired diverticula of the urethra, there was a history of a previous operation on the urethra in sixteen; in the remainder, false passages, blows or falls on the perineum and peri-urethral abscesses are stated as possible causes of the condition.

The diagnosis of a pouch opening into the anterior urethra is as a rule easily made, as the stones which are usually contained in the sac can generally be felt in the perineum. When the sac is not fully occupied by calculi, it may become distended during the act of micturition. The diagnosis is more difficult if the diverticulum is connected with the posterior urethra, although with present day urologic technic it is possible to fill the pouch with a substance that will cast a shadow and which readily outlines the diverticulum.

Calculi in the prostate gland give rise to a sense of weight, pain and irritation in the perineum and sometimes to retention of urine. Crepitation, which may be felt by the examining finger in contact with stones in a pouch, is characteristic and has been compared to "beads in a bag."

When it is possible, an attempt should be made to dissect out the wall of the sac, after it has opened and emptied of its contents. The aperture of communication with the urethra may be closed by suturing lateral flaps, which have been dissected up at the neck of the sac. Usually the most that can be done in the acquired forms of prostatic diverticula is to cut down and evacuate their contents by a median perineal section, a procedure that is sometimes followed by a reformation of stones.

McKay and Colston⁵⁷ found that reported cases of diverticula of the urethra are rare and that in only a few are methods of treatment given. The symptoms of urethral diverticula depend on the site, size, depth and degree of infection. The most obvious symptoms are deep-seated pain in the perineum, dysuria and dribbling at the end of urination. A diverticulum of the anterior urethra often presents a fluctuating tumor that fills during the act of urination and is easily emptied by pressure. A diagnosis is usually made by means of the cysto-urethroscope and the roentgen rays, and the transitory subsiding tumor is occasionally seen.

57. McKay, R. W., and Colston, J. A. C.: Diverticula of the Male Urethra, *Surg. Gynec. Obst.* 48:51, 1929.

If the diverticulum is to be resected, an incision is made over the diverticulum through the skin and subcutaneous tissues. It is then freed by sharp and blunt dissection. It is resected close to its entrance into the urethra, and its stump is turned into the urethra by a purse-string suture, similar to the manner in which the stump of the vermiform appendix is turned in. The purse-string suture is reinforced by bringing the surrounding tissues over by means of mattress sutures. The bladder is drained by an inlying catheter through the urethra; the operative area is not drained, but skin and subcutaneous tissues are closed by fine silk or silver clips.

Another operative procedure described by McKay and Colston is opening the diverticulum into the prostatic urethra, thus making one cavity. This method is applicable only to the diverticula found in the posterior or prostatic urethra. A perineal or suprapubic approach is used with the idea of removing the roof from the diverticulum and converting the cavity of the diverticulum and the cavity of the prostatic urethra into one common opening. This insures proper drainage and also obviates obstruction to urination.

In ten reported cases, seven patients were treated by operative procedures, and one was treated by the injection of silver nitrate. Two patients refused treatment. Only one case was complicated by stone. In the seven cases in which operation was performed, complete resection was done in five, followed by closure of the defect in the urethra over a soft rubber catheter. In four of five patients treated by resection, the diverticula occurred in the anterior urethra, and in one, in the posterior urethra just behind the external sphincter.

Epispadias.—Davis⁵⁸ observed that success has been attained in practically every case in which the surgical procedures in the treatment of epispadias in the female have been properly planned and executed. He stated the belief that it is unnecessary to subject the patient to the risk of ascending renal infection, which is always present after this operation.

Davis employed a two-stage procedure, the second step of which is usually not necessary when the first one is properly carried out. The first stage consists of thoroughgoing plastic repair of the defect. He made a wide exposure of the affected areas, and sufficient and thoroughly controlled excision of excessive mucosa was done under vision. It is important to cut the urethra small enough; if it is too small it can easily be dilated, but if it is too large the operation is a failure and must be repeated. Care should be used in suturing the halves of

⁵⁸ Davis, D. M.: *Epispadias in Females and Its Surgical Treatment*, J. Urol. 20:673, 1928.

the defective internal sphincter muscle over the anterior aspect of the newly formed vesical orifice. The urine should be diverted by a drainage tube in the bladder during the period of healing. If the first step should fail, Deming's gracilis muscle plastic operation is performed. Davis expressed the belief that these methods can be relied on to produce a cure in practically every case of epispadias in the female.

MALIGNANT DISEASE OF THE URINARY TRACT

Barney⁵⁹ stated that hematuria is the most common and often the earliest symptom of malignant disease of the urinary tract. It may be microscopic or macroscopic. It cannot be influenced by medication, and it may not reappear for weeks or months. Pain is not an outstanding feature of malignant disease in this region. It occurs generally at a late stage in the disease and is frequently felt in places other than the primary source. Metastasis from prostatic carcinoma occurs early and often, from the kidney later and less frequently and from the bladder, late and seldom. About one fifth of all cases of prostatic obstruction are associated with carcinoma of the prostate gland. It may not give rise to urinary symptoms.

Early diagnosis of malignant disease of the urinary tract is made with disappointing infrequency, because of the fact that it does not cause outstanding symptoms until well advanced.

URINARY INFECTION

Schlack⁶⁰ reported that in cultures made from 350 specimens of urine of eighty infants, 45 per cent remained sterile. In the non-sterile group, colon bacilli were found in one-third and cocci in the remaining two-thirds. In spite of the finding of bacteria, there was no pyuria. The pyuria may begin with bacteriuria or with symptoms of nephritis.

Experimental and clinical observations on the dehydration types of pyuria are noted but not considered as true infection. They are recognized as renal symptoms, since there are no bacteria present and the cells in the urine are mainly mononuclears, which Schlack assumed came from the renal tubules. In many cases, in spite of early pyuria, the sediment contains mostly mononuclears. Doubtless these cells in the urine are epithelial in origin. Microscopic study of the kidney supports this view.

59. Barney, J. D.: The Early Diagnosis of Malignant Disease of the Urinary Tract, *New England J. Med.* **199**:281, 1928.

60. Schlack, Hans: Zur Pathogenese der Pyurie, *Jahrb. f. Kinderh.* **118**:224, 1927; abstr., *Ztschr. f. urol. Chir.* **24**:363, 1928.

EXTRAVASATION OF URINE

Soloway⁶¹ stated that extravasation of urine is an emergency condition demanding immediate surgical attention. It is caused by stricture of the urethra in most cases and is usually accompanied by a periurethral abscess. In cases of extravasation in which there is no obstruction to urinary outflow, the anaerobic organisms are significant etiologically. The course of the extravasated urine is determined by the relationship between the point of rupture of the urethra and the fascial planes of the perineum. The most common site of rupture is the bulbous urethra, then the membranous urethra, and rarely the prostatic urethra. The physical state of the urine at the time of rupture was observed to play an important part in the course of the condition. Soloway expressed the belief that the best results are obtained by radically opening the focus of infiltration with wide incisions and by rectifying the stricture, when present. Both of these procedures should be done at the same time. Spinal anesthesia has given satisfactory results.

Streptococcus scrotal and penile gangrene and idiopathic gangrene of the scrotum are conditions which closely resemble extravasation and from which it must be distinguished. The prognosis depends on early diagnosis, the duration of the extravasated urine, and immediate radical operation.

URINARY ANTISEPTICS

Voit⁶² conducted experiments to determine whether or not the body disposes of methenamine mainly through the urinary tract or by other means. He found that in the oral administration of methenamine (from 2 to 200 Gm.) free formaldehyde is formed within fifteen minutes; in hyperacidity, it occurs in correspondingly greater amounts. It is to be assumed that this formaldehyde may be lost as far as therapeutic value is concerned, as it is not always found in the urine. Methenamine administered intravenously yields greater quantities and for that reason is found more often in the urine as free formaldehyde.

Further research and animal experimentation have shown that it is excreted by the liver. Voit also showed that it may be excreted by the skin. From these data he concluded that if any therapeutic value is to be obtained by its administration by mouth, large quantities must be given.

FUNCTIONAL TESTS

Bugbee⁶³ stated that renal function is one of the most vital factors influencing the treatment for urologic surgical conditions. Subsequent

⁶¹ Soloway, H. M.: Extravasation of Urine, *J. Urol.* **20**:569, 1928.

⁶² Voit, K.: Untersuchungen über die Ausscheidung von Urotropia, *abstr.*, *Ztschr. f. urol. Chir.* **24**:327, 1928.

⁶³ Bugbee, H. G.: The Role of Kidney Function in Urologic Surgery, *J. Urol.* **20**:541, 1928.

to operation, a continuous knowledge of renal function is of decided value in checking off the progress, estimating the prognosis and influencing the future conduct of the case. Such knowledge is particularly applicable in cases of prostatic obstruction, in which, due to back pressure on the kidneys, congestion soon gives way to renal injury. Dating from the time when regional anesthesia was adopted as a routine measure, in a series of 171 consecutive cases of prostatic obstruction in which treatment was by open operation, only 1 patient (the one hundred and twenty-seventh) died.

Combined estimations of the chemical constituents of the blood and phenolsulphonphthalein have been found satisfactory in determining renal function, but the limitations of either when employed alone have been demonstrated. The observation of a persistently high blood urea has indicated poor renal function. Under reduced protein diet and forced fluids it has been observed that the blood urea often recedes rapidly, while the phenolsulphonphthalein output remains low. In these cases estimations of blood urea alone are of little value, or in combination with the phenolsulphonphthalein test should not influence one against the evidence produced by the phenolsulphonphthalein elimination.

Bugbee attempted to maintain as closely as possible a renal balance throughout. Necessary preliminaries to this end are slow decompression of the bladder, should the residual average be more than 300 cc., and drainage with the indwelling catheter until the function has been stabilized under the relief of back pressure. Bugbee expressed the belief that the type of procedure used in cases of benign hypertrophy of the prostate gland is mainly a matter of personal choice for the operator to decide in the particular case. In his series, if there was the slightest doubt as to the advisability of preliminary cystostomy, this procedure was instituted. In 5 of the 171 cases perineal prostatectomy was done, and in 5, suprapubic prostatectomy in one stage. In 2 cases of carcinoma, only permanent suprapubic drainage was established. In 8 cases a punch operation was adequate after preliminary cystostomy, the prostate gland having become reduced to such an extent that only a fibrous ring remained. Enucleation through a drainage wound is seldom difficult; in none of Bugbee's series was enucleation incomplete or tabs left to interfere with function. There is less tendency to hemorrhage following enucleation after cystostomy drainage, and it is more easily controlled with the hemostatic bag than after the single operation.

Only 4 operative deaths occurred in 181 consecutive operations on the kidney. With due credit to the significance of the early and correct diagnosis of renal lesions, Bugbee considered that a higher mortality was prevented by continued study of the affected kidneys, which largely governed the management of the cases.

TESTS OF RENAL FUNCTION

Maxwell⁶⁴ referred to a study made by MacAdam and Shiskin who found that the cholesterol content of the plasma appears to be a fair measure of the degree of the individual resistance to infection. Such estimations form a useful guide to the degree of operative risk in cases of urinary obstruction. Assuming the lower limit of the plasma cholesterol in health to be 0.13 Gm. per hundred cubic centimeters, they found that of eighteen patients with values below this limit, sixteen died of pyelonephritis and only two recovered. Of the seventy patients with cholesterol values above 0.13 Gm. per hundred cubic centimeters, eleven died, in only one of whom was death a result of ascending urinary infection. It was also noted that, in a large proportion of the cases in which low cholesterol value was found, the clinical condition did not contraindicate operation, and such clinical evidence as there was depended on some degree of defect in renal function rather than on the latent sepsis, from the effects of which the patients ultimately succumbed. MacAdam and Shiskin considered that the test is of much less value in cases of malignant disease, the cholesterol figure being frequently high even when pyelonephritis coexists. Maxwell pointed out that there is a wide variation in the cholesterol content of presumably normal blood figures, varying from 0.08 to 0.23 per hundred cubic centimeters. In this respect it must be clearly recognized that the interpretation of the results of determination of plasma cholesterol differs considerably from that of the other common chemical examinations of the blood. The blood urea and blood sugar have much less variable normal values, and neither is so liable to be affected by a multitude of external factors, partly recognized but still partly unknown, as is the plasma cholesterol. Of five patients with low cholesterol values and who should have been bad risks, two died and three recovered; whereas, of twelve patients with normal cholesterol values, four were clinically unfit for any operation. Three of the remaining eight patients died. Maxwell stated that these results do not bear out the claims of MacAdam and Shiskin as to the significance of the plasma cholesterol from a prognostic point of view.

The chief difficulties in the interpretation of the results appear to be the wide range of variation which may be observed in normal persons and the consequent impossibility of gaging the level in health for any given case. Acute retention of urine appears to have considerably more effect in lowering the plasma cholesterol content than is realized at present, so that deductions should not be drawn from results obtained only previous to the relief of the obstruction.

⁶⁴ Maxwell, James: The Significance of the Blood-Cholesterol in Genito-Urinary Surgery. *Brit. J. Surg.* 16:226, 1928.

The impression gained was that clinical observation, combined with observations on blood urea and urea concentration, yielded in most cases a reasonably accurate forecast of future events. On several occasions a low plasma cholesterol content suggested a bad prognosis, which did not materialize, whereas other patients with normal cholesterol values but who were bad operative risks clinically were either refused operation on clinical grounds alone or died shortly thereafter as a result of some complicating infection.

It would seem that owing to the present rudimentary state of knowledge concerning the cholesterol content of the blood plasma, it is impossible to achieve an accurate summing up, with consequent enlightenment, from the consideration of any individual case. Maxwell expressed the belief that what is really needed is a more intensive study of the normal values obtained in healthy persons, a more complete investigation of the factors causing changes in the plasma cholesterol, and a closer study of cholesterol values and of cholesterol curves in different pathologic states. It would be unjust to refuse operative assistance to any patient suffering from the effects of urinary obstruction merely because on one occasion previous to the proposed operation a low plasma cholesterol value had been reported. Such results are extremely likely to be equivocal, and interpretation is open to fallacy.

(To be continued)

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FINAL REPORT *

EDGAR LORRINGTON GILCREEST, M.D.

SAN FRANCISCO

It is interesting that a condition for which the treatment is purely surgical should have fascinated one of the world's greatest clinicians, who contributed much to the history and to the present scientific knowledge of arteriovenous aneurysm. No physician or surgeon can fail to be thrilled by reading the contributions of Sir William Osler on this subject. Immediately one is impressed with the true catholicity of the pure scientific mind which he possessed. He himself stated: "Better than any other disease, aneurysm illustrates how borderless are the boundaries of medicine and surgery." There is a wealth of meaning to be gleaned in this one sentence in this day of necessary specialization which frequently leads, unfortunately, to a contracted point of view of disease as a whole.

A study of medical history reveals that the aneurysm has had a particular fascination for many of the greatest masters in medicine. The names which come immediately to mind are Rufus of Ephesus and Antyllus in the second century and, later, William and John Hunter. William Hunter, in 1757, was the first to recognize and to describe the symptoms of arteriovenous aneurysm. John Hunter, a few years later, was the first to operate, and successfully, on a patient with this condition. In the present day, William Halsted and Rudolph Matas have added valuable contributions. Although 1,800 years have rolled by, and indeed, much knowledge, bit by bit, has been acquired, surgeons are still searching for additional information in order to explain definitely and finally two questions in physiology: (1) the exact mechanism of the enlargement of the heart, and (2) the retardation of the pulse rate on closure of the arteriovenous fistula.

The answer to this question of the treatment is likewise sought: whether the ligation of the accompanying vein is imperative in an arteriovenous fistula or at least advisable in a simple aneurysm, unless

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* From the University of California Medical School.

* Read before the Southern Surgical Association, Greenbriar Hotel, White Sulphur Springs, W. Va., Dec. 13, 1928.

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The multiplicity of the names for this second group of lesions is often misleading. 1. By arteriovenous aneurysm or varicose aneurysm is meant an indirect communication between an artery and a vein by an intermediary sac or channel. 2. By arteriovenous fistula or aneurysmal varix is meant a direct communication or immediate apposition between an artery and a vein.

The report of the present case is of particular interest because of (1) the duration of the arteriovenous aneurysm; (2) the development of the right side of the chest, the right shoulder girdle and the entire upper right extremity to tremendous size, and (3) data collected before and after operation which add important proof to many of the experimental and clinical observations and the studies of Halsted, Matas, Reid and Holman.

The combination of ligations executed in this case, as far as I can ascertain, has never been used before. James E. Thompson, in 1915, ligated the innominate artery successfully for the cure of a subclavian aneurysm in its first portion. He was able to find authentic references to fifty-two similar ligations in which there were sixteen recoveries, that is, 30.7 per cent. Since 1880, the procedure has been followed twenty-six times, with twelve recoveries and fourteen deaths. As Thompson stated, "This death roll, 53.8 per cent, is enormous, but the disease, is almost certainly fatal sooner or later unless treated by surgical means."

A preliminary report of this case was made on Dec. 8, 1927, before the Western Surgical Association in Omaha. At that time, the patient was clinically well. He has since returned to the hospital and additional distal ligations have been successfully accomplished, with the result that all evidence of the aneurysm has disappeared, his arm has decreased to normal size and he "feels perfectly well." I therefore desire to review the case in full and make a final report.

REPORT OF CASE

A Mexican, aged 35, had been married for seven years and had five children. His wife had had no miscarriages. The patient stated that he had always been

well and strong, and that he did not smoke or drink alcoholic beverages. The only accident which he had ever sustained was the following:

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The wounds were healed in fifteen days. The patient remained in bed about twenty-five days. On the second day after the injury he felt a thrill beneath the right clavicle. The arm was paralyzed and numb immediately after the accident and remained so for four or five weeks. Then there began to be terrific pains and cramps in the entire arm; these gradually lessened. Two or three weeks later the patient was able to move his arm. From the day of injury the arm was swollen and darker than normal. The patient was told by the physician that he had an aneurysm and that he needed an immediate operation. The patient hesitated to have it performed at that time as he desired further consultation.

About Jan. 20, 1921, he returned to his work as bookkeeper. He did not attempt to use his right arm as it was "weak and stiff." He was at this time under no physician's care, and the arm hung limp at his side. He rubbed it frequently to stimulate the circulation. By July, six months after the injury, the pain had subsided a great deal, much strength had returned and there was much better movement of the fingers. The patient now began to work with his right arm and hand. He wrote with it, did bookkeeping and drove an automobile, but he could not use a typewriter or lift any weight. During this time the diseased arm was only slightly larger than the other.

In September, 1921, the patient sought the opinion of a surgeon in Mexico City on account of the increased distention of the veins over the axillary fold and chest. An operation was not advised, and the patient returned home.

From this time until eight months before the first operation, there was little change except that the arm slowly increased in size, and the veins in the axilla and over the anterior part of the chest became more and more distended. During these seven years the patient carried on his regular work about the office and was able to do almost everything except use a typewriter, which was prevented by lack of mobility of the fingers.

About April, 1927, the patient noticed that his entire arm was becoming much larger and heavier, and that he was unable to use it as before. The veins in the upper part of the arm, axilla and chest became more visibly distended. After that time he noticed that if he put his hand down it immediately became much swollen. Also during 1927, he began to have shortness of breath even when standing still in the office. This dyspnea was distressing when he attempted to walk fast or ascend stairs. He found it impossible to run or climb stairs rapidly. He stayed within his reserve and therefore was not compelled to sit down to rest frequently. He never fainted. His sleep was sound and restful. At no time did he have symptoms in the head or notice any swelling of the ankles.

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the hand and fingers prevented any work with the hand. About six weeks before operation the patient also developed two ulcers, one on the dorsum of his hand and the other on the flexor surface of his forearm; these increased in size. As his entire upper right extremity and shoulder had become useless and a burden his physician in Mexico advised him to go to San Francisco and have a shoulder

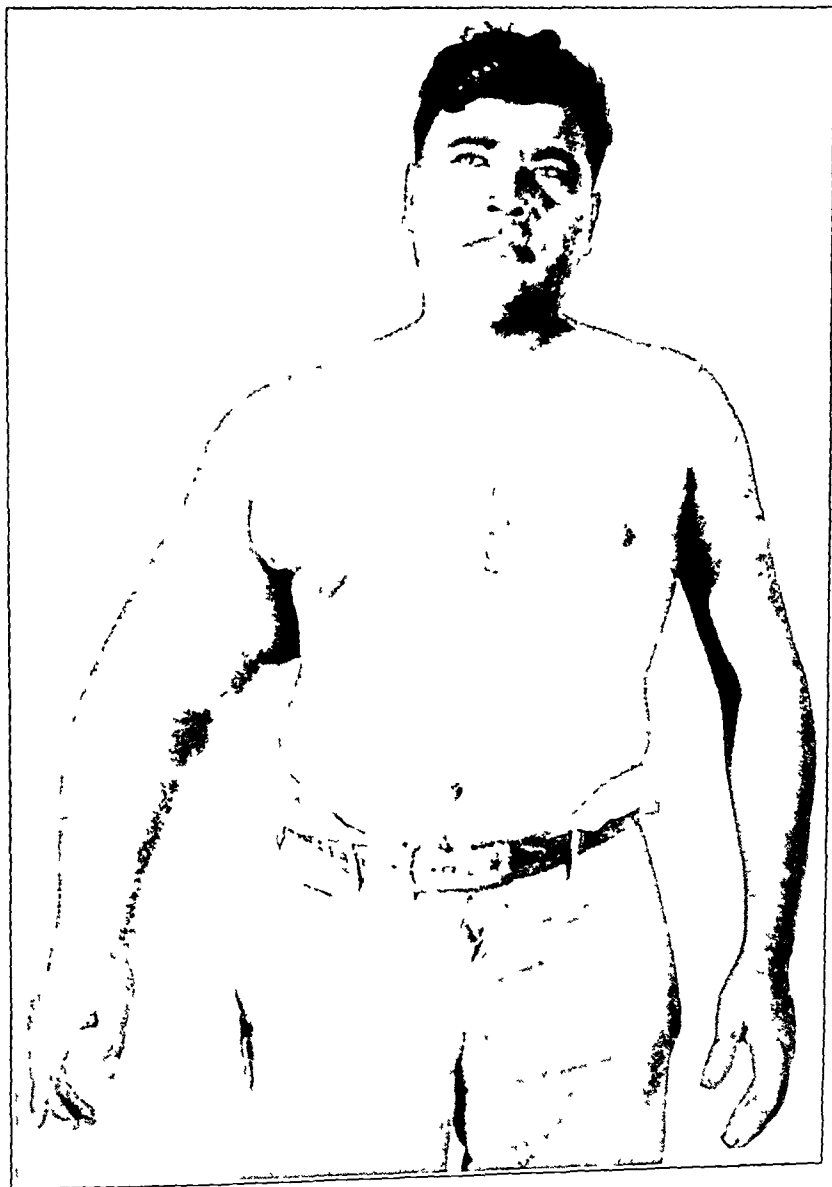


Fig 1 (Sept. 15, 1927)—Traumatic subclavian arteriovenous aneurysm, six weeks before the first operation. Note the great swelling of the upper arm.

girdle amputation. He reconciled himself to this as inevitable and came to me for the operation, being referred by Dr. Frederick Kroll of San Francisco.

It is interesting that during the preceding seven and one-half years no one suggested elevation of the arm or a pressure bandage to relieve the chronic passive congestion with resulting edematous infiltration. During all this time the valves in the veins were gradually giving away.

Examination.—The patient was a remarkably well developed and well nourished man with an extremely broad chest. There was the scar of a bullet wound of entrance over the third costochondral junction to the right, 6 cm. from the middle of the manubrium, and the corresponding scar of a bullet wound of exit over the posterior aspect of the supraclavicular region, 5 cm. from the neck, and just posterior to the lateral edge of the trapezius muscle; the tract apparently traversed the structures underneath the clavicle at its midportion. There was a tremendous swelling, involving the entire right side of the chest wall (fig. 3) including the breast, the right nipple, which was about 3 cm. lower than the left, the pectoral region, the axillary region, and the entire shoulder girdle, arm, forearm and hand (fig. 4). There were large tumor masses, the size of a grapefruit, consisting of huge dilated veins the size of a finger; these were especially visible in the pectoral and axillary region, in the upper third of the arm and along its flexor surface. Although the patient's skin was naturally dark, it was readily seen that the right hand and arm were several shades darker than the left. This darkening of the skin was conspicuous enough to attract the patient's own attention to it. There were two large, indolent, varicose ulcers about 5 by 7 cm. in diameter on the dorsum of the hand and the flexor surface of the forearm.

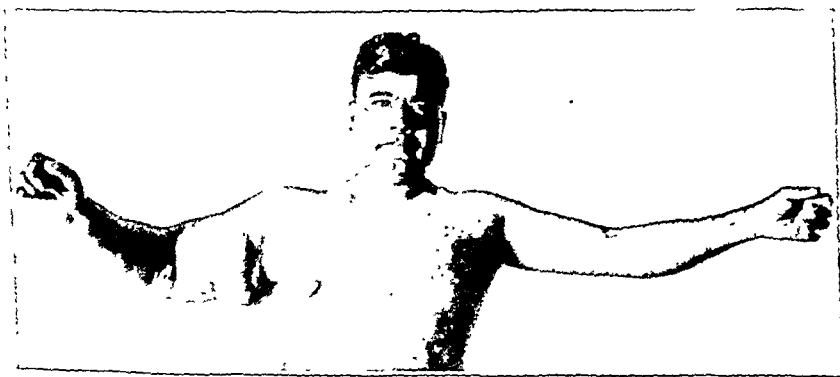


Fig. 2.—Six weeks before the first operation. Note the patient's inability to extend the arm fully.

A systolic thrill was distinctly palpable in the supraclavicular region, less distinctly palpable in the infraclavicular region and distinctly palpable in the axillary region and over the lower third of the inner aspect of the upper arm where the basilic vein courses. Here it was like the purring of a cat.

On auscultation over the right supraclavicular region a continuous booming sound was audible, with systolic accentuation. This bruit was distinctly audible but decreased over the right side of the chest. It was again heard distinctly in the axillary region where it sounded like the murmur of machinery. In fact, the sound was similar to the roar one hears in a subway when a train whirls past. Over the lower third of the arm, where the thrill was most palpable, a loud bruit could be heard with systolic intensification. Here the sound was of a much higher pitch and reminded one of the whistling of the wind. This sound was even transmitted to the upper third of the forearm.

Deep digital pressure applied just above the center of the right clavicle made the thrill imperceptible and the bruit inaudible. On release of the pressure, they instantaneously returned. Presumably this pressure completely obliterated the communication between the subclavian artery and vein. It also produced an

immediate elevation in both diastolic and systolic blood pressure, which rose in the left arm from 134 to 154 systolic and from 74 to 94 diastolic; and a retardation of the pulse from 84 to 76, Branham's bradycardiac reaction. Matas stated: "This is by far the most important and early sign of the cardiovascular disturbances brought about by an arteriovenous fistula and is of great diagnostic significance in all cases in which the arteriovenous connection is accessible to compression." The right radial pulse could be palpated with difficulty. The hand felt cold.

There were no disturbances of motion or sensation in the right arm, with the exception that the great swelling made it impossible for the patient to extend his arm or to flex his fingers completely.



Fig. 3.—Six weeks before the first operation. Note the large lakes of dilated veins over the right side of the chest.

Between the right thumb and index finger the temperature was 35.7 C. and between the left thumb and index finger it was 36.2 C. Examination of the blood showed: hemoglobin, 90 per cent; erythrocytes, 4,800,000; leukocytes, 6,150. The differential count showed: polymorphonuclears, 69 per cent; lymphocytes, 25 per cent; eosinophils, 2 per cent and transitionals 4. The Wassermann test was 4 plus. The urine showed a slight trace of albumin and an occasional hyaline cast.

Blood from a vein of the right arm gave an oxygen content of 11.4 per cent by volume and from the left arm 69 per cent by volume; blood from a vein of the right arm gave a carbon dioxide content of 38 per cent by volume, and from the left arm 49.4 per cent by volume.

On Nov. 3, 1927, a 6 foot (1.8 meters) ventral projection showed the heart definitely increased above normal size. The enlargement seemed to affect the left ventricle predominantly. The aorta was neither elongated nor dilated. The right side of the chest was a little less well expanded than the left in its upper portion.

Diagnosis.—The lesion was diagnosed as an arteriovenous aneurysm of the subclavian artery and vein, rather than a simple aneurysm. This conclusion was based on the following factors: (1) the great swelling of the arm, (2) the great dilatation of the veins, (3) the continuous purring thrill, (4) the continuous buzzing or machinery-like murmur accentuated during systole, (5) the centrifugal

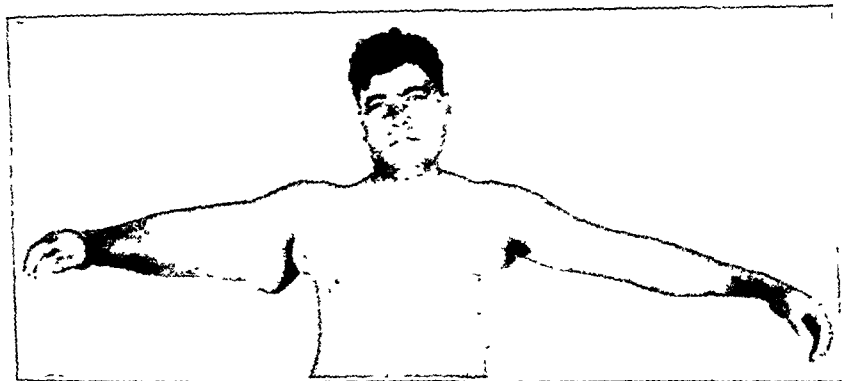


Fig. 4.—Six weeks before the first operation. Note the great swelling also of the forearm and hand.

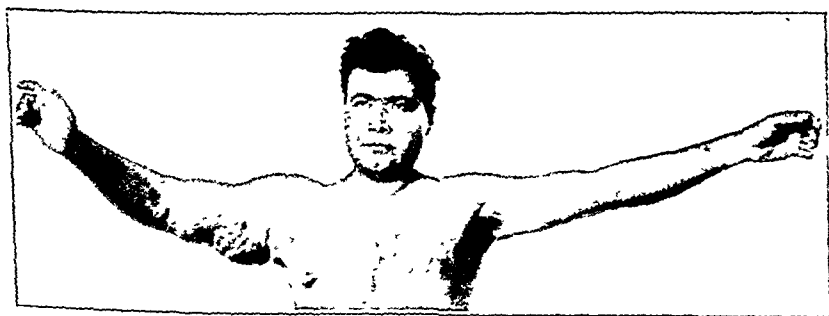


Fig. 5 (Nov. 4, 1927).—One day before the first operation. Note the decrease in swelling after six weeks of elevation and the application of an elastic bandage.

transmission of the bruit and thrill along the course of the axillary and basilic veins, (6) the elevation of blood pressure on temporary deep pressure over the site of the lesion, (7) the retardation of the pulse on temporary deep pressure over the site of the lesion, (8) the increase of oxygen content in the veins of the right arm, (9) the decrease in local temperature and (10) the enlargement of the heart.

For several weeks prior to the operation the patient was kept in bed; his right arm was elevated in a Thomas splint and crepe bandages were applied to the entire arm and shoulder girdle. This proved effectual in decreasing a great deal of the edema. It also afforded the heart a necessary rest (fig. 5).

The plan of operation consisted of the following steps: (1) subperiosteal resection of the proximal two thirds of the clavicle, (2) transection of the muscles of the neck, permitting thereby: (3) the free exposure of the great vessels of the upper part of the chest and neck, (4) possible ligation of the innominate artery and vein and the carotid artery and jugular vein, (5) or ligation of the subclavian artery and vein; and (6) further, if practicable, ligation of the artery and vein distal to, and as close to, the sac as possible, but proximal to the origin of the posterior circumflex and subscapular vessels—in short, a quadruple ligation of the fistula or aneurysm.

This procedure was carried out twice on a cadaver previous to the operation.

The operation was performed on Nov. 5, 1927, at 9:30 a. m. Forty-five minutes before the operation, the patient was given a hypodermic injection of $\frac{1}{4}$ grain (16 mg.) of morphine and $\frac{1}{150}$ grain (0.4 mg.) of atropine. He was placed on the table with shoulders and head slightly elevated; the head was slightly extended and turned to the left side. Local anesthesia of 0.5 per cent procaine hydrochloride was given. This was first injected near the angle of the jaw and just under the chin in the midline in order to apply the towel skin clips without hurting the patient. Starting at a point between the articulation of the clavicle to the manubrium, procaine hydrochloride was injected 3 cm. to the left and over the right clavicle to its outer third and from the manubrium up along the anterior border of the sternomastoid muscle for 7 cm. An incision was now made from the outer third of the right clavicle and slightly below it, and extended up along the anterior border of the right sternomastoid muscle for 8 cm. The skin flap was dissected in both directions. The sternomastoid muscle was divided. The triangular flap of skin and muscle was turned upward and outward. The external jugular vein was ligated.

The sternohyoid and sternothyroid muscles were severed about 1.5 cm. above the sternum and laid back. A subperiosteal resection of the inner two thirds of the clavicle was carried out; it was cut through with a Gigli saw and disarticulated at the sternum. With this exposure the large mass of dilated veins under the clavicle and over the arteriovenous aneurysm, as well as the large vessels of the neck, came clearly into view (fig. 6). The arteriovenous aneurysm involved the second and third portions of the subclavian artery and vein. It should be recalled that the subclavian artery and vein are not companionate in their first part but are separated by the anterior scalene muscle. The mass of large veins over the aneurysm were adherent to each other and to all the surrounding tissues. One of the larger veins, thought to be the subclavian, was ligated at its outer third, as a thrill could be felt over the proximal area.

Gas and ether were administered at 10:30 a. m. The carotid artery was located with the adjacent vagus nerve and dissected down along the anterior and inner surface until the subclavian artery could be felt coming up from behind and bifurcating with it at an acute angle. The subclavian artery was then followed up. It was seen to be enlarged and to emerge into the aneurysm in its second portion. The subclavian vein in nearly its entirety was part of the aneurysm, the remaining proximal end being greatly dilated. For this reason it was decided to ligate the innominate vein. Then the internal jugular was ligated, medium braided silk being used for the ligations. In attempting to push the pleura downward and outward in order to free the subclavian artery, a slight tear occurred in it producing a slight pneumothorax. Contrary to the observation of most authors, the first portion of the subclavian artery was not found difficult to ligate. Heavy braided silk was used and a double ligation was performed after the method of Ballance and Edmunds. With the exposure obtained, one could dis-

tinctly see the best site for the ligation and could feel sure that the recurrent laryngeal nerve was not incorporated in the ligature.

No thrill could be felt now, but as there was still some dilation of the veins over the aneurysmal varix, one of the large veins toward the distal portion was ligated. In attempting to free this large vessel with its thin wall from the adherent tissue and veins, and to pass the aneurysm needle around it some venous hemorrhage occurred which was fairly easily controlled. The mass immediately became smaller with the ligation of this vessel, which was thought to be the subclavian vein. In all, I ligated the innominate vein, the external jugular and the internal

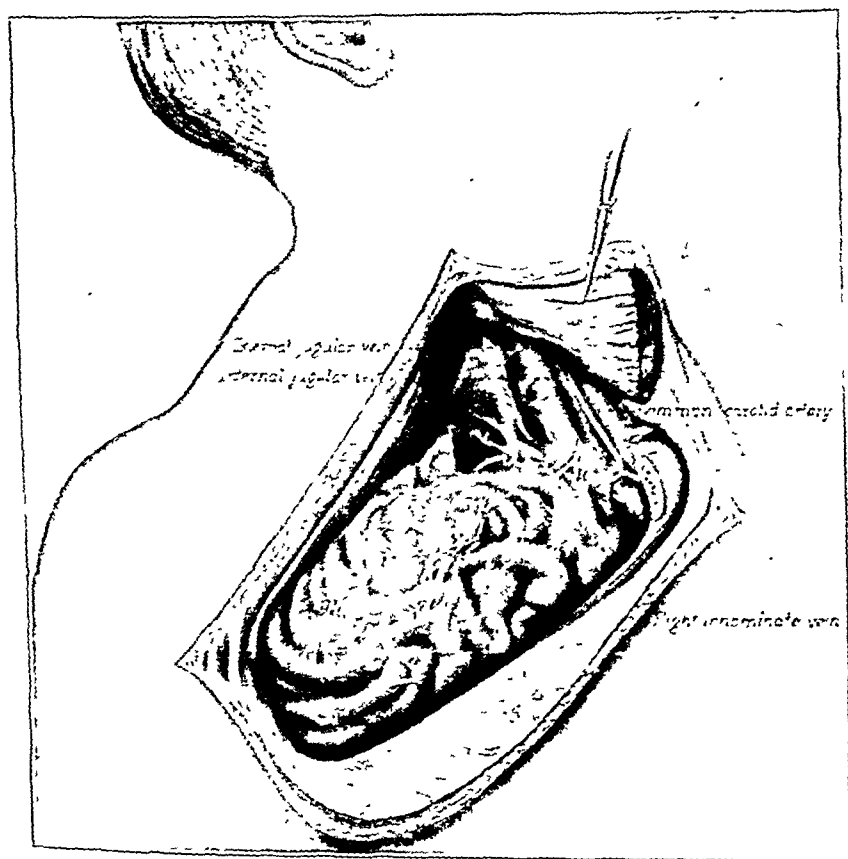


Fig. 6.—Great mass of dilated veins beneath the clavicle. The aneurysm is between the subclavian artery and vein.

jugular veins, the subclavian vein in two places and the subclavian artery in its first portion (fig. 7).

The question that naturally presented itself then was whether to attempt further dissection through this veritable wilderness of matted dilated thin-walled veins and to execute a distal ligation of the artery and vein, that is, the third part of the subclavian artery and vein or the axillary artery and vein with a possibility of dissecting out completely the aneurysmal sac, or to rest on the laurels won. As the procedure had already consumed more than three hours and as no thrill could now be felt nor bruit heard, it was decided to adopt the latter course, in the hope that with the aid of these ligations nature might close the fistula, if any

remained. The severed muscles were brought in apposition and sutured, and the wound was sutured in layers without drainage.

Postoperative Progress.—The patient manifested practically no evidence of shock. The wound healed per primam. Some swelling in the right supraclavicular space was observed on the sixth day, when the stitches were removed. This was due to an accumulation of serum which was aspirated on the eighth, tenth, thirteenth and twenty-first days after the operation. The fluid did not return.

The blood pressure which previous to operation was 134 systolic and 74 diastolic was 136 systolic and 74 diastolic one hour later. The next day, it was 150 systolic

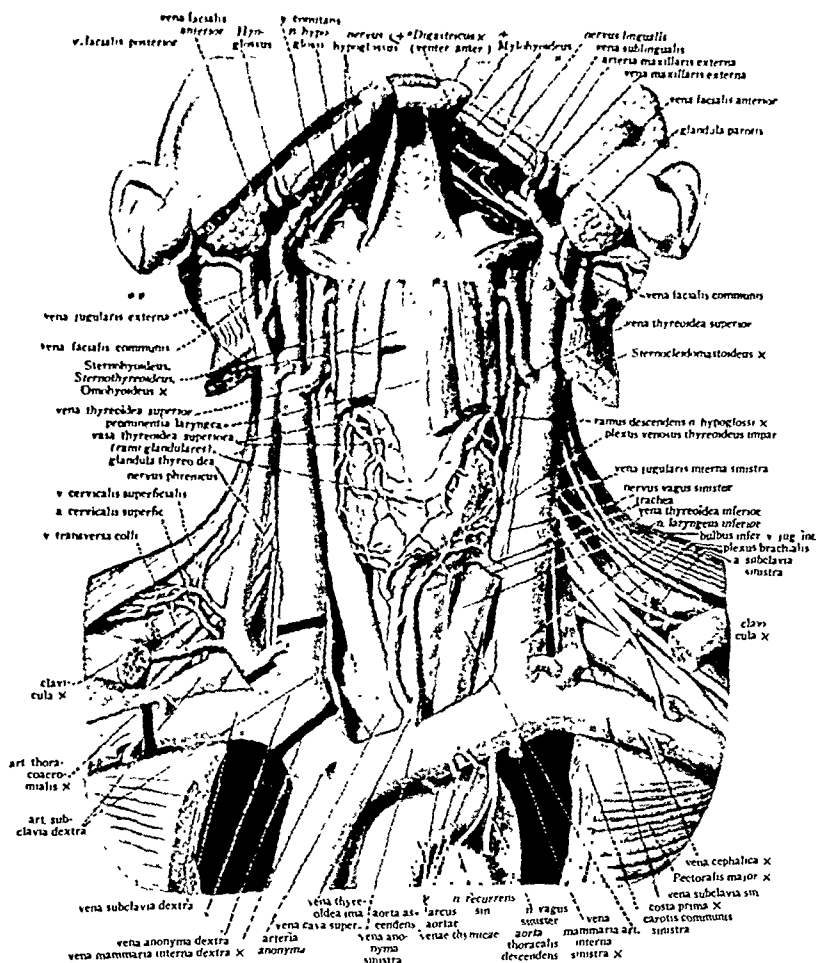


Fig. 7.—Sites of the ligation of the external and internal jugular, subclavian and innominate veins and the subclavian artery. (From Sabota's Anatomy.)

and 112 diastolic; two days later, 152 systolic and 86 diastolic, and the third day, 164 systolic and 82 diastolic; it then gradually declined until on the twenty-eighth day it was 124 systolic and 74 diastolic.

The day following the operation, the patient complained of severe pain in the lower right anterior axillary region when an attempt was made to change his position or to move his right arm. On the tenth day the classic signs of fluid were present in the right lower portion of the chest, and a roentgenogram revealed a fluid line. A thoracentesis was performed on the fifteenth and seventeenth days, but only on the latter day were 2 ounces of sanguineous fluid aspirated. This was repeated on the twentieth day with the same success. Two days later no fluid

could be seen in the chest. The lung, which had been collapsed, due to the pneumothorax, was now expanded. The diaphragm was high and did not move, indicating that the right phrenic nerve had been injured.

A diminution in the size of the right side of the chest, the entire shoulder girdle, arm, forearm and hand was conspicuous after the second day, and continued uninterruptedly, as shown by the accompanying table of circumferential measurements (table 1). This decrease in the venous channels is of particular interest when it is remembered that the innominate, subclavian and jugular veins were ligated.

On Dec. 5, 1927, twenty-eight days after operation, the patient was feeling well. The swelling of the arm was decreasing steadily (fig. 8). The bruit was becoming less and less distinct. Only a slight thrill was palpable. The patient returned to his home in Mexico that day.

Whether in this case a quadruple ligation should have been carried out at this time, thereby subjecting the patient to considerable additional risk, deserves consideration. Time will best answer this question. While the surgeon should be daring he must never lack restraint. If I had performed this operation, there

TABLE 1.—Circumferential Measurements During the First Stage of Treatment, 1927

	Oct. 29	Oct. 25	Nov. 14	Nov. 12	Nov. 24	Dec. 5
Area	Cm.	Cm.	Cm.	Cm.	Cm.	Cm.
Wrist	19.25	18	18	17.25	17.0	16.5
Middle forearm, 14 cm. above wrist.....	32.0	29	26	25.0	25.0	24.5
Elbow	40.0	34	33	32.0	31.0	29.5
Middle arm just below greatest swelling.....	52.0	43	42	41.0	39.5	38.0
Over greatest swelling, upper third of arm...	55.0	51	49	47.0	43.5	41.0
Axilla	53.0	50	47	45.0	45.5	44.0
Around shoulder girdle, 9 cm. from nipple....	66.0	61	60	55.0	55.0	54.0
Right side of chest at level of midline.....	68.0	64	56	53.0	53.0	52.5
Left side of chest at level of midline.....	50.0	50	50	50.0	50.0	50.0

would have been no opportunity to see what nature could do in finally closing the fistula or aneurysm when partial ligation had been accomplished. As Halsted said, "Surgeons should bear always in mind the opportunities which they have daily at the operative table to strive for results which may be contributory to the advancement of their science. The operating room is a laboratory for the surgeon."

Second Admission.—On Aug. 6, 1928, the patient was readmitted to the hospital, stating that he had felt perfectly well since the first operation on Nov. 5, 1927. He had been working regularly, using both arms and hands with ease. The great swelling of his shoulder, arm and hand had not returned. Seven weeks before the second admission, however, with the advent of very warm weather, he noticed that the veins in the axilla became larger. Coincidentally, a varicose ulcer developed over the flexor surface of the right forearm. Six days before, he had awakened during the night to find that a considerable hemorrhage had occurred in this ulcer and that he was lying in a pool of blood. During the next five minutes he continued to bleed so profusely, that he thought he would die. Pressure controlled the hemorrhage, however, and he left Mexico the next day for San Francisco.

Examination.—Examination (fig. 9) at this time revealed a slight increase in the swelling of the right shoulder girdle and arm, but there was no return of the

great swelling seen prior to the first operation. The patient was able to slip his arm into his coat sleeve and he walked about with ease. The circumferential measurements are shown in table 2.

Over the flexor surface of the midportion of the forearm there was an ulcer, 3 cm. in diameter, surrounded by markedly discolored skin and an induration of the soft tissue. In fact, the entire right arm and hand were much darker than the left. No pulse could be felt at the right wrist. There was no impairment of motion or sensation at any point. The clavicle, the inner half of which was removed, showed definite regeneration.

Just above this regenerated clavicle, at its midpoint, there was still a thrill on deep palpation. This thrill could also be felt on deep palpation in the axilla over



Fig. 8 (Dec. 5, 1927).—One month after the first operation. Note the great reduction in the swelling of the right side of the chest and the entire right arm.

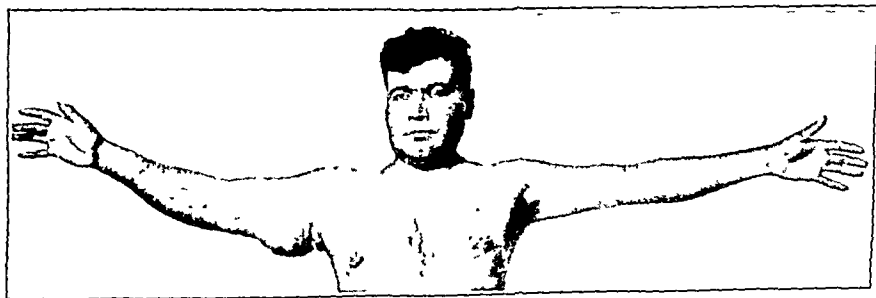


Fig. 9.—Note the gradual recurrence of the swelling, nine months after the first operation.

the mass of tortuous large veins which lay just underneath the skin. There was a point just above the elbow where the thrill was distinctly felt and heard on auscultation. Deep pressure above the clavicle resulted in a complete disappearance of the thrill and bruit and visible recession in the size of the dilated veins in the axilla. Before the closure of the fistula the blood pressure in the left arm was 140 systolic and 82 diastolic. On closing the fistula the blood pressure immediately rose to 158 systolic and 90 diastolic, dropping as long as the fistula was closed to 150 systolic. Accompanying this increase in blood pressure, there was a slowing of the pulse from 72 to 64. The heart sounds were normal. The apex beat could barely be felt in the nipple line. There was no increase in precordial activity and the heart was not demonstrably enlarged to percussion.

The hemoglobin was 90.5; the red cells, 4,900,000 and the white cells, 9,900. The Wassermann reaction was 3 plus.

Examination of the urine revealed a slight trace of albumin.

On Aug. 8, 1928, the right leaf of the diaphragm was still very high, the dome reaching just above the fifth rib anteriorly. It was not quite so high as on Dec. 1, 1927.

The heart was still large; it appeared appreciably larger than on Nov. 3, 1927, before the first operation. Measurement of the shadow of the heart vessel by planimeter showed that on Nov. 3, 1927, it was 189 sq. cm., and at the time of the second admission it was 198.3 sq. cm. Apparently the high diaphragm produced a torsion of the heart with a greater apparent than actual increase in size.

It was quite evident that the condition was an arteriovenous aneurysm which had reestablished itself following ligation of the subclavian artery in its first portion and ligation of the innominate, subclavian and jugular veins about eight months before.

Operation.—It was decided: (1) to resect the completely regenerated inner portion and outer third of the clavicle which was still intact; (2) to expose the axillary vessels beyond the communication between the vessels, which lay probably in the third portion of the subclavian artery; (3) to identify the structures distal to the fistula, and (4) to expose the aneurysm itself, separate the vessels, preserve the artery and vein, if possible, and if not, excise the aneurysm.

Operation was performed on Aug. 10, 1928, at 9 a. m. Gas anesthesia was used throughout the operation. The patient was placed in position with the arm at right angles to the body, and the shoulders slightly elevated. An incision was made along the line of the old scar extending laterally to the coraco-acromial articulation. The regenerated portion of the clavicle was removed as well as about 2.5 inches (6.3 cm.) of the intact clavicle. Numerous dilated veins were encountered in approaching the clavicle. Whether it was due to the position of the arm it is difficult to say, but it was almost impossible to palpate the thrill which previously had seemed quite prominent over the center of the clavicle. There was no pulsation to be felt in any of the vessels except in the common carotid artery on the right side. Identification of structure was extremely difficult, primarily because of this absence of the thrill and pulsation; the scar tissue resulting from the previous operation still further obscured the normal tissue. It was felt wise to continue the dissection down the arm in an endeavor to expose normal tissue and then work back toward the supposed location of the communication. The subclavius muscle was divided as was a considerable portion of the pectoralis major.

After some difficulty the axillary vein was finally identified. This hugely dilated vein had a diameter of 2.5 cm. On further exposure the vein was found to be pulsating; closure of it resulted in the identification of the aneurysmal sac about the size of an English walnut which lay just below and posterior to the middle of the clavicle. A faint thrill could be felt over this aneurysmal sac which was completely controlled by closure of the axillary vein beyond it. Closely adherent to this sac, just superior to the axillary vein were cords of the brachial plexus; these, in turn, surrounded the axillary artery which at this point was approximately 4 mm. in diameter. There was no pulsation to be felt in this axillary artery beyond the aneurysmal sac. This resulted in a considerable delay in its exact identification. The ligation of the axillary vein with a piece of narrow tape produced a conspicuous and easily palpable pulsation of the aneurysmal sac. An attempt was then made to find the arterial connections with this sac, but

pressure at any particular point failed to influence the pulsation greatly. The subclavian artery was identified, lying just posterior to the scalenus anticus muscle (fig. 10).

It is interesting to note that this artery was not palpable before ligation of the axillary vein, primarily because of the large venous reservoir into which it emptied. Closure of the subclavian artery just beyond its emergence from the scalenus muscle resulted in a marked diminution in pulsation, but not in the complete

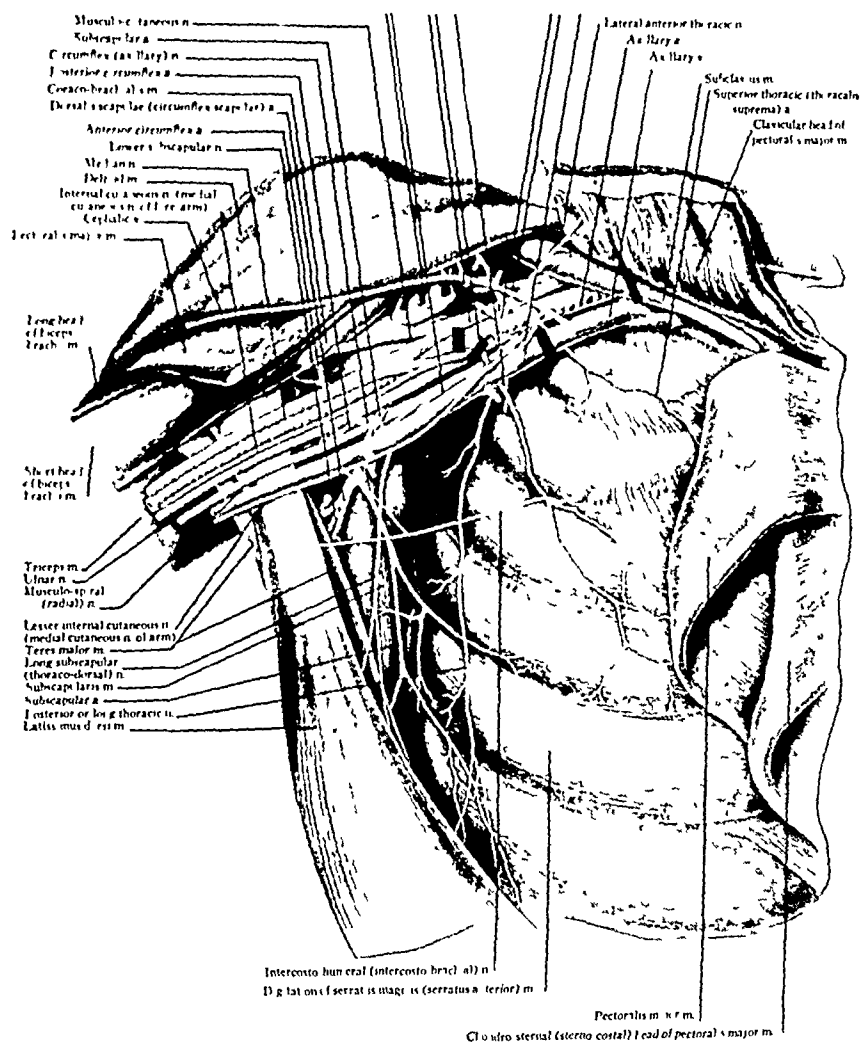


Fig. 10.—Sites of ligation of the axillary and long thoracic veins, and the subclavian, axillary and long thoracic arteries. (From Deaver's Surgical Anatomy.)

control of the arterial supply of the sac. It was ligated with braided silk. The axillary artery was ligated with silk, with a little further diminution of the pulsation of the sac. The long thoracic artery and vein lying posterior to the axillary vein were also ligated with braided silk. This controlled the pulsation of the sac almost completely. It was felt, however, that with ligation of the axillary vein and almost complete control of arterial supply, the aneurysmal sac would probably be closed by thrombosis. It was thought that the subclavian

artery in its third portion emptied almost completely into this aneurysmal sac which in turn emptied into the very large axillary vein. It is worthy of mention that when the axillary vein was ligated, the general blood pressure rose about 10 points. All bleeding points were controlled during the operation with sutures and ligatures of silk. The cephalic vein was dilated to a diameter of about 1 cm. The subcutaneous tissue and skin were closed with interrupted sutures of silk.

Immediately after the operation the hand which formerly had felt cold now had good color and was warm. There was unquestionably an immediate improvement in the circulation through the procedure followed.

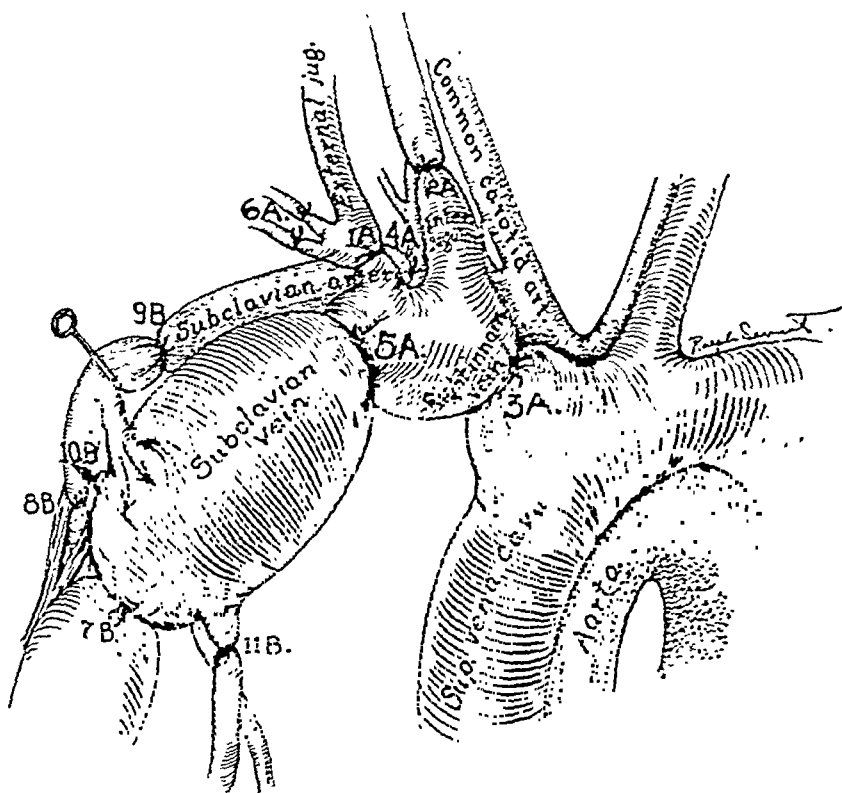


Fig. 11.—The operation as completed in two stages. The ligatures are numbered in the order of their application.

The great difficulty encountered in the second operation, which was tedious and required six hours, was further proof that it would have been inadvisable to have attempted more at the first operation.

The ligations during the first operation were of the external and internal jugular, subclavian and innominate veins and the subclavian artery; and during the second operation of the axillary and long thoracic veins and subclavian, axillary and long thoracic arteries, a total of ten ligations (fig. 11).

Postoperative Notes.—On Aug. 11, 1928, the first dressing was applied.

On August 11, 3 a. m.: The patient felt well. There was no pain in the right hand or arm, which seemed even warmer than the other. The dressings which were loose were removed: a slight serosanguineous discharge was noted. The tissues were quite boggy in the region of the wound, suggesting edema. During

the operation it was noted that there were frequent little bursts of clear fluid into the wounds, apparently from dilated lymph vessels. The patient complained of being hot. Examination revealed a blood pressure of 170 systolic and 110 diastolic. A dry dressing was applied.

August 11, 10 a. m.: The wound was dressed. There was boggy swelling, suggesting accumulation of fluid in the wound. A probe was introduced into the wound and a considerable amount of almost clear fluid was evacuated. A dry dressing was applied. The blood pressure was 136 systolic and 84 diastolic. It was evident that the peak of the postoperative rise in blood pressure would have been missed if a reading had not been made during the night (3 a. m.). The pulse in the right radial artery was easily palpable for the first time since the patient was first seen; the rate was 84.

August 12: The dressing had to be changed on two occasions because of the marked serous discharge from the wound. No bleeding occurred. A few stitches were removed. The blood pressure was 164 systolic and 86 diastolic; the pulse was 86.

August 13: The remaining stitches were removed. The wound was in good condition, and no discharge had occurred since the day before. Apparently, there

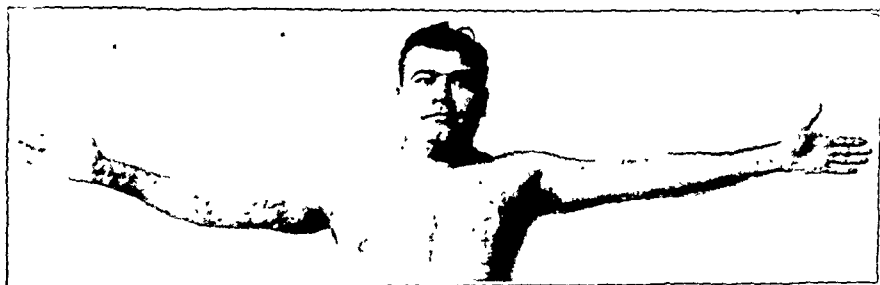


Fig. 12 (November, 1928).—Complete cure, three months after the second operation. The circumferential measurements of both arms is the same. The patient writes, "I am feeling perfectly well."

was no further fling up of the wound. The blood pressure was 166 systolic and 84 diastolic; the pulse rate was 88. A dressing was applied.

From this time on, the progress of the patient was uneventful, with the exception of the development of an extensive thrombophlebitis of the veins of the anterior wall of the chest and of the upper arm. The condition subsided with rest in bed, immobilization of the arm and hot fomentations.

September 12: The patient left for Mexico. No thrill could be felt nor bruit heard. The shoulder and arm were steadily decreasing in size. The patient was feeling stronger daily. The blood pressure was 130 systolic and 86 diastolic. The pulse rate was 76.

November 11: The patient wrote: "I am feeling perfectly well and my arm is recovering its life. It is a little stiff but its size is normal at this time, as you will notice from the enclosed picture" (fig. 12).

COMMENT

Thompson, in his classic monograph on subclavian aneurysm, said that "ligature of the first part of the subclavian artery has turned out to be a very unsatisfactory operation. It is both difficult and dangerous.

The artery is very short, numerous branches arise from it, it is very deeply situated and is surrounded by important veins and nerves. The internal jugular and vertebral veins are directly in front of it; also the pneumogastric and phrenic nerves. At its origin, the right innominate vein forms an anterior relationship." I believe that the reason this procedure has proved so difficult is that the surgeon has attempted this ligation without first performing a subperiosteal resection of the inner half of the clavicle. By this step, a very difficult approach is rendered much more accessible.

In an arteriovenous fistula the pulse is smaller on the injured side showing that the volume of arterial blood is less, while the dilated veins show that the venous blood is increased.

The retardation of the pulse rate on closure of the fistula by digital pressure or by permanent suture or ligation was explained by Holman as follows: "Closure of the fistula results in a filling up of the aorta by the volume of blood which formerly leaked through into the veins.

TABLE 2—Circumferential Measurements During Second Stage of Treatment, 1928

	Jan 2	Feb. 28	Aug. 6	Nov 12
Area	Cm.	Cm.	Cm.	Cm.
Wrist	17.0	17.0	17.0	16.5
Middle forearm, 14 cm. above the wrist	28.0	28.0	27.0	24.0
Elbow	32.0	32.0	32.0	28.0
Middle arm just below greatest swelling	38.0	38.0	37.5	31.5
Over greatest swelling upper third arm.	41.0	41.0	41.0	35.5
Axilla	45.0	45.0	45.0	42.5
Right side of chest at level of midline	52.5	52.5	54.0	54.0
Left side of chest at level of midline	51.0	51.0	52.5	52.0

This produces an increase in aortic pressure which in turn stimulates the depressor fibers of the vagus in the arch of the aorta and reflex slowing of the heart is the result."

Holman and Dock have definitely shown, in experimenting with animals, that in an arteriovenous fistula the cardiac output is doubled. This observation is interesting as it differs from that of Lewis who stated "that the output in an arteriovenous fistula does not appear to be unusually altered."

Holman was among the first to emphasize the physiologic basis for the alteration in blood pressure by opening and closing the fistula, giving as his explanation an increase in the total volume of blood during the existence of the fistula.

Conditions in the fistula that determine or influence the systemic effects are, according to Matas: (a) the size of the arteriovenous fistula; (b) the volume and force of the arterial stream that is short-circuited into the communicating vein; (c) the caliber of the vessels involved; (d) the proximity to the heart; (e) the duration of the fistula; (f) the age of the patient, and (g) the coexistence of the antecedent cardiovascular disease.

It is always to be remembered that gangrene occurs much more frequently in an arteriovenous than in a saccular aneurysm. I believe that in an arteriovenous aneurysm simultaneous ligation of the accompanying vein with the artery should always be executed. This would appear at first thought to be paradoxical. Indeed, it reverses a surgical principle long emphasized by writers of textbooks. The special needle or ligature carrier was invented with the main idea of being able to ligate the artery safely without injury to the satellite vein. To ligate unhesitatingly a normal and large vein is contrary to tradition. Tradition is not easy to set aside.

I believe, however, that there is now sufficient experimental and clinical proof that this procedure today should be a recognized rule. Professor Tuffier, the great French surgeon, said that "ligation of the correspondingly healthy vein" should be executed "in all cases of ligation of the great vessels of the root of the limbs." Sir George Makins, the eminent British surgeon, long an authority in surgery of blood vessels, stated that "the elimination, in fact, of the capacious main vein is a real advantage, since this for the time affords a too ready channel of exit for the diminished arterial supply, as well as an undesirable reservoir for stagnation." He concluded, "these considerations have led me not only to regard obligatory simultaneous occlusion of a main artery and vein as a negligible factor in the risk of gangrene of a limb; but to hold further, that the procedure is preferable whether the vein be wounded or not; the result of the combined procedure being to maintain within the limb for a longer period the smaller amount of blood supplied by the collateral arterial circulation, and hence to improve the conditions necessary for the preservation of the vitality of the limb." In accord with this procedure but disagreeing with Makin's explanation, Brooks and Martin stated that the increase in the peripheral blood pressure is the principal beneficial result of ligating the vein. Reid and Holman's observations support the latter view. Holman, in his brilliant experimental work, repeatedly proved the necessity of this simultaneous ligation of vein and artery.

In the light of this knowledge one must accept the view that some degree of equilibrium of the arterial and venous systems must be preserved. I believe that the following maxims may be laid down for the prevention of gangrene: 1. In an arteriovenous fistula or aneurysm it is imperative to ligate the accompanying vein if the artery is ligated. 2. In a simple aneurysm it is at least advisable to do so.

Few or none of these patients should be operated on until from three to six months have expired unless the cardiovascular effects are conspicuous and progressive. Then if the fistula still exists, further delay is not indicated. The reasons for waiting are (*a*) the possibility of a spontaneous closure of the artificial communication with cure, and

(b) the possibility of awakening a lurking infection if the operation follows the injury too soon. Infection usually results in death.

"Common errors in the treatment of aneurysms," according to Halsted, "are the following: (1) opening the sac or pulsating hematoma without first making a temporary occlusion of all the possible sources of hemorrhage; (2) the permanent ligation of a great arterial trunk as a precautionary measure in the search for a distal bleeding point; (3) ligation of a trunk too far from the aneurysm; (4) stuffing the wound with gauze to arrest hemorrhage; (5) drainage; (6) the employment of catgut for the ligature, or of silk that is too fine, and (7) ligation of the artery proximal to an arteriovenous aneurysm or fistula."

Surgeons attempting to intervene in aneurysms or arteriovenous fistulas should be much more concerned with hemostasis and meticulous technic than with the duration of the operation. These operations are at best always tedious and time-robbing and demand the best of the surgeon's skill. Without profuse hemorrhage these patients stand operations of six or seven hours' duration without severe shock. "An operator searching for a bleeding point in a pool of blood, and particularly so when embarrassed in his movements by the adherent walls of an aneurysm within which he is working so disadvantageously, presents a distressing spectacle. I would rather devote an additional hour or more to an operation than be caught for a few moments in such a predicament" (Halsted). The reestablishment of a normal vascular equilibrium is the objective sought.

SUMMARY

A case of traumatic subclavian arteriovenous aneurysm of eight years' duration showed:

1. Enormous swelling of the right side of the chest, the right portion of the shoulder girdle and the entire right arm and hand, with great distention of veins in these parts.
2. Cardiac dilatation and hypertrophy resulting from increased volume flow through the heart incident to the production of the fistula.
3. Branham's bradycardiac reaction and associated variations in blood pressure due to an increase in blood volume caused by the fistula.
4. Characteristic bruit and thrill transmitted centrifugally.
5. Increase of oxygen content in veins distal to lesion.
6. Dilation of the proximal artery, diminution of the distal artery and great dilatation and thickening of the distal vein.
7. That proximal ligations of artery and veins improved the condition but did not effect a cure.
8. That subsequent distal ligations, ten months later, completing the quadruple ligation, effected a cure.

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8. That subsequent distal ligations, ten months later, completing the quadruple ligation, effected a cure.

ABSTRACT OF DISCUSSION

DR. HERMANN B. GESSNER, New Orleans: Dr. Gilcreest is to be congratulated, not only on the skill with which he treated this patient, but on the thoroughness with which he reviewed the symptomatology and pathology of the condition. In my experience with arteriovenous aneurysms, which has been limited to those of the lower extremity, I have been able in some cases to control the fistula by attacking it from the venous side. I remember one interesting case in which the vein involved was a vena comes. I was able to incise the vein, suture the orifice with paraffinized silk, and then sacrifice the vena comes.

I think one diagnostic sign is worth bringing out. Dr. Gilcreest did not mention it, probably because the diagnosis in his case was so clear. I refer to the sign I have learned from my teacher and friend, Dr. Rudolph Matas: It is the change in the distal pulse, the Delbet sign. I can recall two cases in which the diagnosis was made in that way. One was a case of aneurysm of the popliteal artery. No bruit was discernible. A mass was present. It was not possible to find the pulsation of the tibial arteries. I presented this patient to a class and Dr. Matas operated, confirming the diagnosis. The explanation was simple. The aneurysm was so filled with clot that there was little movement of blood.

In a case of aneurysm of the forearm seen recently, the patient had a hematoma that permitted the diagnosis by means of a needle. There was no pulsation and no bruit; yet, on incising the hematoma, arterial blood came out, escaping from a wound of the radial artery. I think it important to realize that aneurysms may be recognized on this Delbet sign.

It happens not infrequently that an aneurysm is incised under the diagnosis of abscess. I know of a case in which an aneurysm of the subclavian artery was incised in that way. The patient had pain and tenderness, a rise in temperature and leukocytosis. A colleague of mine opened the aneurysm in the belief that it was an abscess. I think this diagnostic point should be brought out and carefully considered, as tending to prevent such errors.

DR. ALBERT O. SINGLETON, Galveston, Texas: Through his persistence in this case Dr. Gilcreest has obtained an excellent result. Arteriovenous aneurysms are more of a problem than the sacculated aneurysms. Probably in Dr. Gilcreest's case he performed part of the operation and hoped for success, and then did the other part subsequently, rather than completing it all at once. He has shown that the operation took a long time, and I do not think that he is necessarily a slow operator. Any one who has operated in these cases realizes that although time passes rapidly, the surgeon often does not get far.

I appreciate Dr. Gessner's remarks about the diagnosis, and think they should be repeated often. In the usual run of work, these cases are not seen frequently, and these points are sometimes forgotten. The aneurysm varix has an opening, which makes the problem more difficult than in the case in which Dr. Gessner was able to suture the aneurysm from within the vein. I have been helped in two or three cases in making a differential diagnosis between aneurysm varix and arteriovenous aneurysm by injecting sodium iodide into the artery, and then making a roentgenogram to show the direct communication. This method also shows the collateral circulation in its approximation to the sac. In one case it showed that there was a considerable interval and a sac between the artery and the vein.

Dr. Gilcreest, I think, is right in ligating the vein at the same time as the artery. I had a patient with an aneurysm at the lowest part of the external iliac artery, on which I intended to perform a double ligation. On exposing it, however, above the aneurysm and clamping the artery I saw such an immediate blanching of

the foot that it was evident that an ischemic gangrene would probably develop if I ligated the artery alone. On clamping the vein, the warmth of the foot promptly returned. I ended by ligating both of the vessels, and the circulation was not much interfered with. The leg remained warm and continued warm until a subsequent ligation resulted in a perfect cure.

DR. W. LOWNDES PEPLE, Richmond, Va.: I also wish to congratulate Dr. Gilcreest on his perseverance and success, and wish to show you a recent case of aneurysm of the femoral artery, which occurred in a man about 22 years old, who had been shot with a 22 caliber rifle about ten years before. He was not ill at the time, there was no swelling, he resumed all of his activities, athletics and so forth, and had no trouble for nine years. He then began to have attacks of pain in the region of his heart. Six weeks before his admission to the hospital he had violent pain over the region of the iliac artery. All of the typical signs and symptoms of a fistula were obtained. The x-ray picture showed an enormously large artery pulled to one side, the femoral vein accompanying it also pulled to one side, and the vein which lay beneath it was visible. One could see the small aneurysm, about the size of a pigeon's egg. It was as though the drift of the arterial blood driven across the vein has caused this sacculatation. The man was a good patient, young, strong and thin; it was possible, therefore, to ligate the artery above and below, and ligate the normal femoral vein above and below. We then dissected out the sac. There were several veins opening into this which were easily tied.

I am glad to see that the other speakers have no doubts whatever about the advisability of ligating even the normal accompanying vein. This seems to be now an ordinary procedure, which one might speak of as stabilization of the vein. There was no reaction in the dorsalis pedis artery or the posterior tibia which was apparently normal on both sides. The patient made an uneventful recovery.

DR. J. L. CAMPBELL, Atlanta, Ga.: I suppose that the surgical division of the Grady Hospital is the best place in the world to find injuries to blood vessels. I recall twenty-five or thirty patients who have been operated on for this condition in my service, and most of these cases were of the arteriovenous type. I operated on a patient for subclavian aneurysm a number of years ago, and am glad to know that Dr. Gilcreest recommends resection of the clavicle. I do not think that one can operate adequately without this space. In my case I succeeded in curing the patient, in whom the condition was quite recent, by proximal ligation. The patient was a negro and I was unable to keep track of him.

The next case was that of an aneurysm of the common carotid artery in which an arteriovenous aneurysm had occurred. In that case I succeeded in restoring both vessels and the patient recovered.

The next case was that of a subclavian aneurysm in which I attempted to restore the lumen of both vessels. I had just the condition that Dr. Peple showed, with dilation of the vein. I applied a suture and attempted to make the separation so that I could close it. The patient became weak and the anesthetist said that I had better stop. Unfortunately, the patient died. That is the only patient that I have lost.

I have had two cases of aneurysm of the profunda and two of the femoral artery. In one of these I attempted to restore the lumen of the vessel, and gangrene resulted. In the other case I did not see the patient until after the limb had been amputated. I have had one aneurysm at the bend of the elbow, and two or three in the popliteal space. When the patients are seen early I think proximodistal ligation should be performed. If they are seen later, but when the vessels can be cleared and the patient is in good condition, I think that the

lumen can be restored without much difficulty. In one case of a pulsating exophthalmos I succeeded in partially occluding the internal carotid artery with a band, and relieved the patient of all his symptoms.

These cases are interesting. Any time the physicians present happen to be in Atlanta, I shall be glad to show them some of the cases. There nearly always are several in the hospital.

DR. GEORGE TULLY VAUGHAN, Washington, D. C.: I listened with great pleasure to Dr. Gilcreest's account, for I have had much experience with aneurysms of various kinds. Dr. Campbell just said that he was foolish enough to try to close the wounds and vessels in one patient and the patient died. Perhaps if he had closed the wounds the patient would not have died. I was foolish enough to try the same thing a number of years ago. A patient had just been shot through Scarpa's triangle. The injury happened on a street car and someone stuck a handkerchief into the wound. I watched the case and for two weeks there was no sign. Then an aneurysm varix developed, with a bruit. I operated and found a wound in the vein and artery, also four points in vessels filled with lymph. I closed these openings with fine vaselized sutures. The patient is living today, after fourteen years, and has no trouble with his extremities.

So many surgeons have spoken of the necessity of ligating both vessels, that they occlude the veins. This may be necessary occasionally, but not always. I have operated on many patients and have performed the Matas operation on several occasions, filling in the walls of the vessel sac so as to close the vessel completely, and not touching the vein. I have done this on the external iliac, the iliac, and on the femoral arteries and have not seen a case of gangrene. I have had probably a dozen cases of this kind.

I wish to ask Dr. Gilcreest why he did not find the openings in these two vessels and sew them up instead of using so many ligatures.

DR. WALTER C. G. KIRCHNER, St. Louis: I wish to congratulate the essayist on this splendid piece of surgery. Three years ago I ligated a subclavian artery in the first portion, I wish to mention a few points in differential diagnosis. This case was also a gunshot wound, the aneurysm having enlarged and become engorged on the vessels of the neck. It was present on the left side. There was no pulsation in the right pulse. There was atrophy on the one side, in addition to the enlargement on the other. In other respects there were all the characteristic signs of aneurysm. Careful dissection was made under general anesthesia. It was possible to ligate the first portion of the subclavian artery near the aortic arch without resecting the clavicle. In fact, that was the easiest part of the operation. The more difficult part, a fact that I can appreciate greatly, is the opening of the sac and the treatment of the condition when the hemorrhage is present. Unless one has had that experience he cannot realize how difficult it is to find these structures. In the aneurysm there is a lot of fibrous tissue and a lot of disarrangement of structures. This explains why so much time is necessary in handling these cases.

DR. GILCREEST: I am naturally pleased that the report of this case excited such extensive discussion.

Referring to Dr. Gessner's mention of Delbet's sign, it will interest him to know that the patient's radial pulse was practically imperceptible, which is consistent with what Dr. Gessner pointed out; it became palpable only after the second operation.

I am glad to note that Dr. Singleton also appreciated that to carry out this technic correctly consumes much time. The cases reported by him and Dr. Peple are of great clinical significance.

The large series of operations by Dr. Campbell are most unusual. I do not know anywhere in the country where such a wealth of records of vascular surgical procedures could be found. I shall indeed avail myself of Dr. Campbell's invitation to see some of these patients the first time I revisit Atlanta.

Answering Dr. Vaughan's question of why I did not find the openings into the arteries and veins and sew them up, instead of resorting to so many ligatures, I can only repeat what I said before, that to have attempted this procedure through such a wilderness of large dilated thin-walled veins would have been only to produce profuse hemorrhage and court disaster. Dr. Kirchner emphasized this in his remarks.

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THE CELIAC PLEXUS AND ITS BRANCHES *

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Modern surgery through the use of local anesthesia has focused attention on the celiac plexus. At first, the chief concern was merely to develop a technic for making injections into this plexus which would permit the carrying out of certain major operations under local anesthesia. This led to the recording of new observations concerning its physiology. Relatively little attention has been paid, however, to the exact macroscopic and microscopic appearance of this region in the light of recent surgical experiences. Some of the disturbances referable to the duodenum and the pancreas which make their appearance after operations on the gallbladder and other abdominal operations require an exact anatomic knowledge of the celiac plexus for their proper understanding. So, too, attacks of abdominal pain simulating pain due to gallstones can be better differentiated from pancreatic, celiac and other types of medical and surgical pain, if one appreciates more fully the histologic character and ramifications of this plexus.

The modern surgeon still refers to the anatomic plates of the celiac plexus executed during the past century by Hirschfeld-Leveillé,¹ Henle,² Testut,³ Poirier,⁴ Quain⁵ and others, since nowhere in the newer literature is there to be found any record of a recent systematic investigation of the plexus as a whole. Even the work of Hirt⁶ (1924) is concerned only with the innervation of the kidney and the suprarenal gland, while Raigorodsky⁷ (1928) described only the branches of the

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5. Quain: *Elements of Anatomy*, London, Longmans, Green & Company, 1896-1900.

6. Hirt: *Vergleichend-anatomische Untersuchungen über die Innervation der Niere*, Ztschr. f. Anat. u. Entwgesch. **73**:621, 1924.

7. Raigorodsky: *Die Nerven der Leberpforte des Menschen*, Ztschr. f. d. ges. Anat. **86**:698, 1928.

hepatic plexus. The well known illustrations which are to be found in textbooks give, in general, a clear idea of the topography of the branches of the plexus. But they are more or less schematic, do not concern the innervation of the pancreas and the duodenum and do not treat of the plexus in relation to surgical procedures.

This stimulated us to investigate the celiac plexus from the standpoint of modern surgery, which we did with the help of the newest macrotechnical methods. We carried out our investigations on thin adult human cadavers. In animals, the topography and distribution of the plexus are extremely variable, so that the anatomic relationships, as well as the physiologic results, obtained from dissections and investigations carried out on animals cannot be compared with those obtained in man. It has been our aim in this study to present a systematic description of the plexuses and their connections without exact reference to topographic details.

TECHNIC

We dissected under slowly dripping water, and we also employed the acidol pepsin digestion method with good results.⁸ The dissection was also carried out on specimens that were not fixed and which were kept in cold running water during a period often of from two to three days or more. This loosened the collagen fibers. The cleanly prepared nerves were later colored by the method described by Gyermek⁹ of this institute in 1919.

In the preparation of fine nerves there is always the danger of calling adjacent lymph vessels, small veins and connective tissue fibers, nerves. To avoid this, we compared several specimens prepared one after another, and controlled the relation of the nerves, as well as of the ganglions, with one another.

In addition to the celiac ganglions, well known treatises also describe the celiac plexus, which they consider the central part of the whole system. The following are mentioned as individual parts of the plexus which go to the various organs: (1) plexus phrenicus or plexus diaphragmaticus, (2) plexus aorticus, (3) plexus suprarenalis, (4) plexus renalis, (5) plexus spermaticus, (6) plexus gastricus superior and inferior, (7) plexus hepaticus, (8) plexus lienalis, (9) plexus mesentericus superior, (10) plexus mesentericus inferior and (11) plexus pancreaticus. We, for the most part, employ this grouping.

In our description, we will consider: (1) the celiac ganglions, (2) the roots of the celiac ganglions, (3) the branches of the celiac ganglions and (4) the microscopic structure of the celiac plexus.

8. Two pastils of strong acidol pepsin are dissolved in 200 cc. of water. The field of dissection is kept well moistened with this solution. It is applied either by tampons or by pipet and, if necessary, over a period of from two to three hours. This makes the removal of connective tissues considerably easier.

9. Gyermek: *Farben makroskopisch-anatomischer Präparate*, Ztschr. f. wissenschaftl. Mikr. **35**:45, 1918.

THE CELIAC GANGLIONS

In most instances, we found a flat ganglion the size of a strawberry on each side of the celiac artery (figs. 1, 2 and 3), the form of which may be variable. We sometimes found two, three or more smaller ganglions on each side (fig. 4). The ganglions on one side are united to those on the other by many transverse fibers above and below the celiac artery, in front of the aorta (fig. 1). In the majority of cases, however, an unpaired ganglion lies under the celiac ganglions directly on the aorta (fig. 3 18). Many authors call this ganglion the ganglion aorticum or, because of its union with the renal plexus, the ganglion aorticorenale. The other ganglions in this region, which we have illustrated in our figures, belong to the diaphragmatic and renal plexuses. The celiac ganglions form the central point for the celiac plexus.

THE ROOTS OF THE CELIAC PLEXUS

The roots of the celiac plexus are formed by the nervi splanchnici majores and minores and both vagi. Figures 1 and 2 and figure 3 2 and 2a show clearly the course of the splanchnic nerves. It is of practical importance to note the lengthy course (from 8 to 10 cm.) of the nervus splanchnicus major (fig. 3 2) behind the lumbar portion of the diaphragm. Surgical procedures also make use of this fact. Thus, the splanchnic nerves are infiltrated transdiaphragmatically in the space between the vertebral column and the lumbar portion of the diaphragm. In that the splanchnic minor (fig. 3 2a) lies close to the splanchnic major, it is of course blocked by the same injection. In this way (as will be seen in the paragraph dealing with the microscopic structure of the plexus), all the sensory roots of the celiac plexus are blocked. Figure 3 3 shows that after the splanchnic major perforates the diaphragm, it then turns in a right angle medially and ends in the celiac ganglion.

One reads in most textbooks (for example, that of Spalteholz¹⁰) that the left vagus does not always take part in the formation of the celiac plexus. We, however, found in every specimen that both vagi contributed many branches to the formation of the plexus (fig. 1 3).

Spalteholz pointed out that the upper lumbar ganglions of the sympathetic send fibers to the plexus. Because of the proximity of the plexus to the ganglions, this would seem quite possible. We found no such branches.

THE BRANCHES OF THE CELIAC PLEXUS

We desire to draw special attention to the linking branches between the celiac ganglions of both sides (fig. 1) which lie in front of the

10. Spalteholz: Handatlas der Anatomie des Menschen, Leipzig, S. Hirzel, 1895-1903.

aorta, surround the celiac artery and form a dense plexus. The older descriptions lead one to the erroneous belief that both celiac ganglions sometimes form a single semilunar ganglion. We did not observe this in any specimen. As we have already pointed out, the celiac ganglions form with their branches the center and chief plexus of nerves going to the abdominal organs. The splanchnic nerves enter the ganglions, while the fibers of both vagi either end in these linking branches or run direct to the plexuses in the organs. All sympathetic and sensory fibers of the celiac plexus arise either from the ganglion bodies or from the linking branches. This explains why infiltration of the celiac ganglions results in complete anesthesia of the area between the diaphragm and the pelvis.

We refer briefly to the following plexuses of nerves going to the various abdominal organs.

Plexus Phrenicus (figs. 1 and 2).—This small plexus lies on the anterior part of the lumbar portion of the diaphragm in the region of the inferior phrenic artery. The roots of this plexus arise directly from the celiac ganglions. We found the ganglion phrenicum, which is the size of a small pea, on both sides (fig. 1 12). On the left side, the ganglion phrenicum lies in closer relation to the celiac ganglion. Luschka,¹¹ in 1853, described the relation of this ganglion with the phrenic plexus and phrenic nerve. We observed the same relationship in every specimen. But the phrenic plexus and the sympathetic nervous system play no part in the motor innervation of the diaphragm. Our microscopic investigations have shown that the branches of this plexus consist mostly of nonmedullated sympathetic fibers, and that between the sympathetic fibers only solitary medullated fibers are to be seen. The sympathetic fibers run to blood vessels and to the suprarenal glands, while the medullated fibers unite the region of the celiac plexus with the phrenic nerve and through the phrenic nerve with the cervical plexus. This is the route through which "pain" from the region of the celiac plexus (liver, pancreas, kidney, stomach and intestinal canal) reaches the plexus in the cervical region and produces reflex pain in the shoulder. In support of our observation is also the fact that, after splanchnic anesthesia, the movement of the diaphragm is in no way affected either by the development of a partial paralysis or by other functional disturbances.¹²

Plexus Suprarenalis (figs. 1 13 and 2 9a).—The many roots of this plexus arise from the celiac ganglion and from the phrenic and renal plexuses. We found no macroscopic ganglions in this plexus. Accord-

11. Luschka: Nervus Phrenicus, Tübingen, H. Laupp, 1853.

12. Kiss and Ballou: Contribution to the Nerve Supply of the Diaphragm, Anat. Rec. 41:285, 1929.

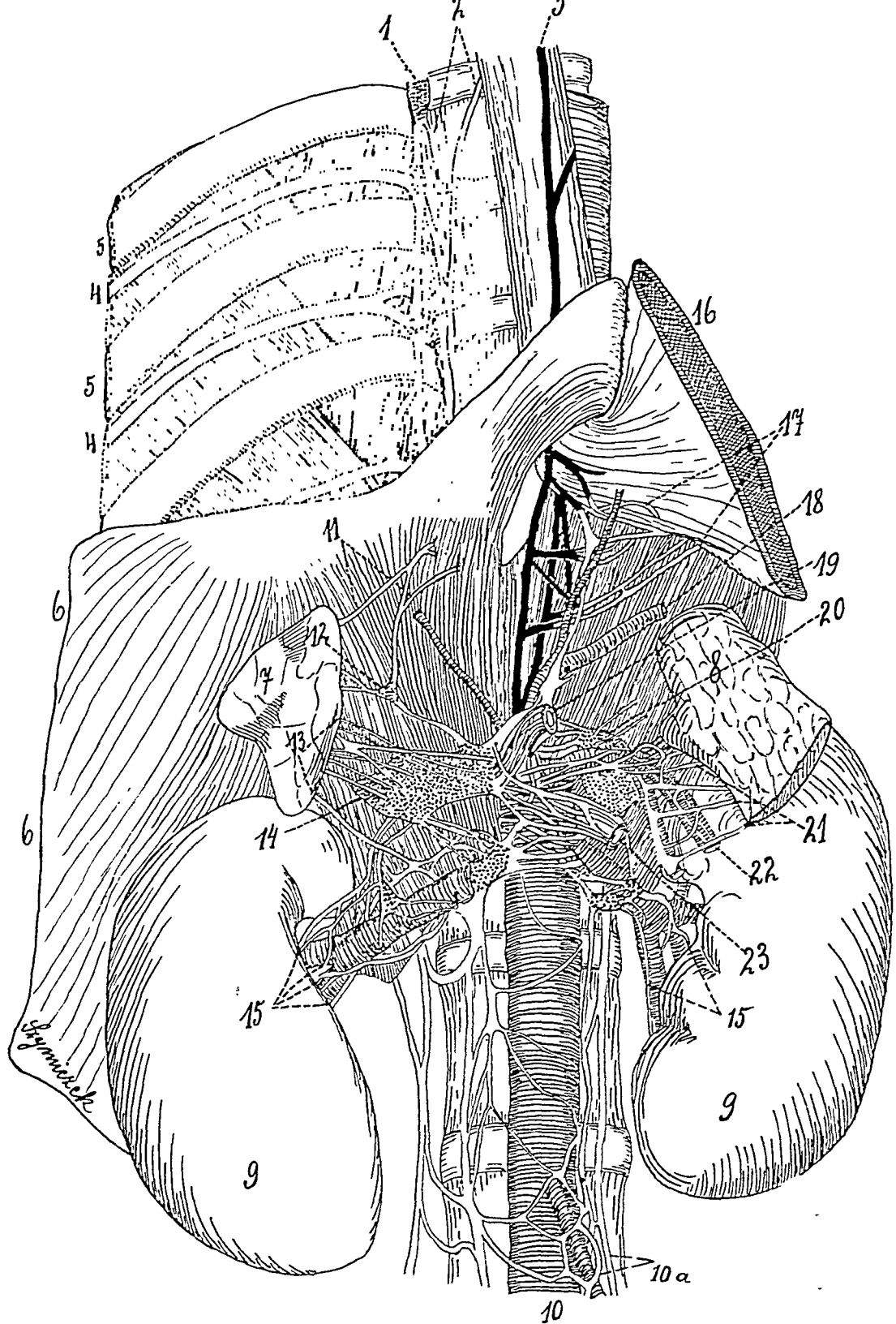


Fig. 1.—Plexus coeliacus (splanchnic—deep level). Figures 1 and 2 are taken at different levels. 1 indicates truncus sympathicus; 2, nervus splanchnicus major; 3, nervus vagus (right); 4, nervi intercostales; 5, ribs; 6, diaphragm; 7, suprarenal gland (right); 8, pancreas (body), retracted to the left; 9, kidney; 10, plexus aorticus; 10a, aorta; 11, plexus phrenicus (diaphragmaticus); 12, ganglion phrenicum; 13, plexus suprarenalis; 14, ganglion coeliacum (right); 15, plexus renalis and renal artery; 16, cardia ventriculi; 17, plexus cardiacus; 18, gastric artery (left); 19, plexus coeliacus and coeliac artery; 20, ganglion coeliacum (left); 21, plexus pancreatis (left portion); 22, plexus lienalis and splenic artery, and 23, plexus mesentericus superior and superior mesenteric artery.

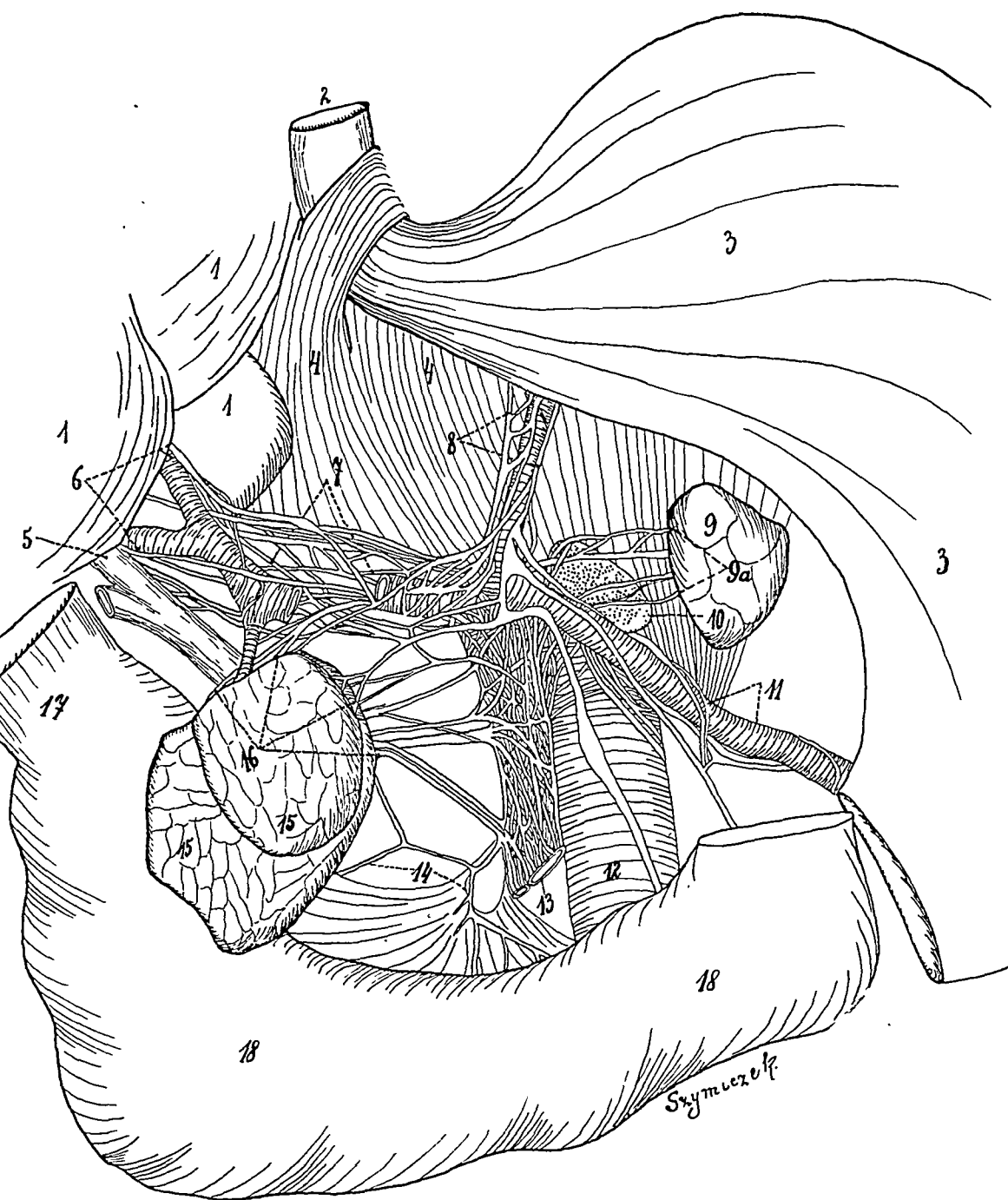


Fig. 2.—Plexus coeliacus (superficial level). 1 indicates liver, lobus caudatus (Spigelii); 2, esophagus; 3, stomach; 4, diaphragm; 5, ductus hepaticus; 6, hepatic artery; 7, plexus hepaticus; 8, plexus cardiacus; 9, suprarenal gland (left); 9a, plexus suprarenalis sinister; 10, ganglion coeliacum sinister; 11, plexus lienalis and splenic artery; 12, aorta; 13, plexus mesentericus superior and superior mesenteric artery; 14, plexus duodenalis (in part); 15, caput pancreatis; 16, plexus pancreatis (right portion); 17, pylorus, and 18, duodenum.

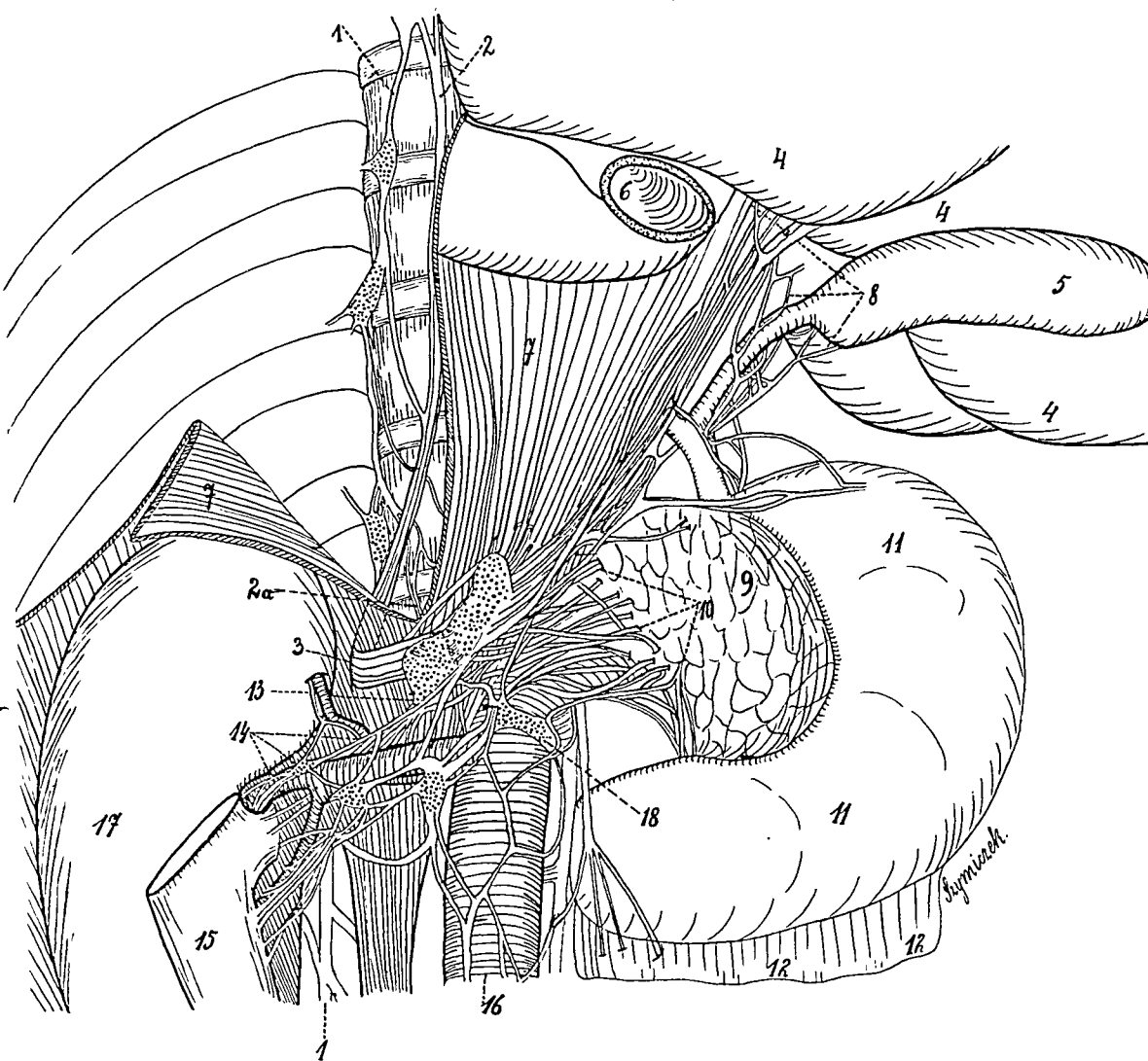


Fig. 3.—Plexus coeliacus, seen from the right. 1 indicates truncus sympathicus dexter; 2, nervus splanchnicus major; 2a, nervus splanchnicus minor; 3, nervus splanchnicus major perforating the diaphragm; 4, liver; 5, gallbladder (pulled to left); 6, vena cava inferior; 7, diaphragm (lumbar portion); 8, plexus hepaticus (posterior view); 9, caput pancreatis (pulled over to left); 10, plexus pancreatis (posterior view); 11, duodenum (pulled to left, posterior view); 12, peritoneal covering of duodenum; 13, ganglion coeliacum dexter; 14, plexus renalis dexter and renal artery; 15, vena cava inferior (pulled to right, posterior view); 16, aorta with plexus aorticus; 17, kidney (right), and 18, ganglion aorticum.

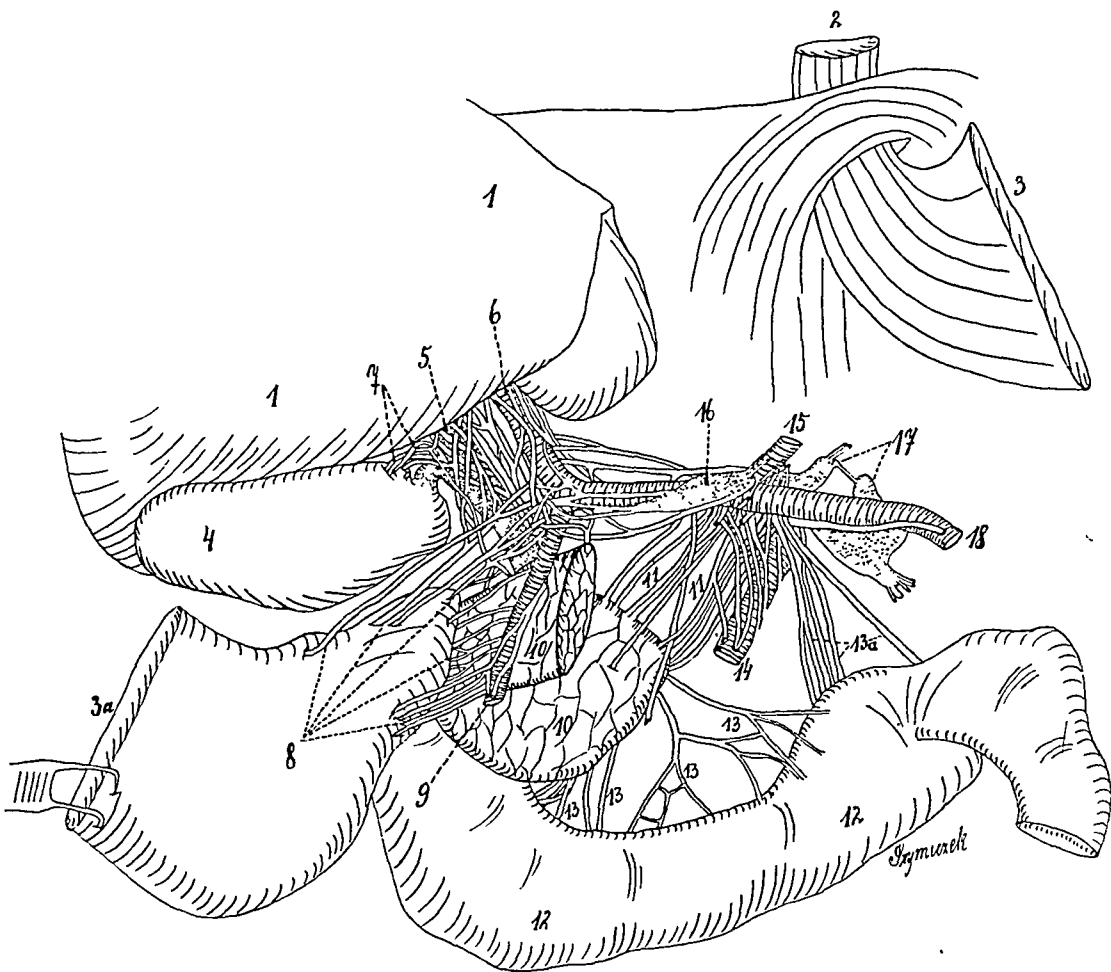


Fig. 4.—Plexus hepaticus, pancreaticus and duodenalis. 1 indicates liver; 2, esophagus; 3, stomach, cardia; 3a, pylorus; 4, gallbladder; 5, ductus hepaticus and plexus hepaticus; 6, hepatic artery and plexus hepaticus; 7, plexus cysticus; 8, plexus py'oricus; 9, gastroduodenal artery; 10, caput pancreatis; 11, plexus pancreaticus; 12, duodenum; 13, plexus duodenalis; 13a, plexus duodenalis (left portion); 14, plexus mesentericus superior and superior mesenteric artery; 15, gastric artery (left); 16, ganglion coeliacum dexter; 17, ganglion coeliacum sinister, and 18, splenic artery.

ing to Hirt,⁶ the individual fibers of the plexus run through the left suprarenal gland toward the renal cortex.

Plexus Renalis (figs. 1 15 and 3 14).—The roots of this plexus arise from the celiac ganglion, from the uniting branches between the right and the left celiac ganglions and from the aortic plexus. We always found several ganglions in the plexus, varying in size from that of a millet seed to that of a pea. The branches follow the renal arteries.

Plexus Aorticus (figs. 1 10 and 3 16).—This is a dense plexus on both sides of the abdominal aorta with many linking branches between both sides. Its chief branches arise from both trunks of the sympathetic, from the celiac plexus and from both renal plexuses. The aortic plexus sends branches to the inferior mesenteric plexus and to the spermatic plexus (latter not illustrated in the figures).

Plexus Cardiacus and Plexus Pyloricus (figs. 1 17, 2 8, 4 8 and 5 1).—The descriptions hitherto make mention of a gastric plexus or a superior and an inferior gastric plexus. We constantly found that the nerves reach the stomach at the cardia and at the pylorus, so that it is preferable to speak of a cardiac and a pyloric plexus.

The cardiac plexus is formed by branches of both vagi and by branches from the celiac plexus. Accessory branches come from the celiac ganglions, from its uniting branches and from the hepatic plexus. It forms a small plexus, which encircles the gastric artery, and which runs to the cardiac portion of the stomach. Here it meets the branches of both vagi.

The pyloric plexus (fig. 4 8) comes from the hepatic plexus and from the plexus that winds around the gastroduodenal artery (fig. 4 9). The roots of the last mentioned plexus arise partly from the hepatic plexus and partly directly from the celiac plexus. The branches penetrate obliquely into the wall of the stomach.

We do not wish to make any lengthy clinical digressions in this report. But the description that has been given suggests that certain derangements after operations on the stomach may be explained on a purely anatomic basis, particularly the normal correlated action of pylorus and cardia. When one appreciates that gastrojejunal ulcer develops more frequently when a gastro-enterostomy has been performed on a normal stomach than when it has been performed for ulcer, and that amputation neuromas may be demonstrated at the base of gastric ulcers, then it seems not unlikely that at least some of the disturbances noted, particularly after extensive operations on the stomach, are to be attributed to the destruction of important nerve fibers. This may be caused either directly through degeneration of nerve fibers or indirectly by the formation of scars. Certain it is, however, that extensive resec-

tions of the stomach are not possible without destruction of important nerve fibers.

Plexus Lienalis (figs. 1 22, 2 11 and 4 18).—The roots of this plexus come from the celiac plexus, from the cardiac plexus and from the superior mesenteric plexus. Single branches come directly from the left celiac ganglions. The splenic plexus directs itself with the splenic artery to the spleen. On its way, this plexus gives off many branches to the pancreas (fig. 1 21). We found no macroscopic ganglions in this plexus.

Hepatic Plexus (figs. 2 7, 3 8, 4 5, 6 and 7 and 5 4).—The hepatic plexus is a rich plexus that lies in the hepatoduodenal ligament, and surrounds the hepatic artery, portal vein, hepatic duct and common bile duct. As many fibers run anteriorly to these structures as posteriorly; for this reason Raigorodsky,⁷ in a new description, distinguished an anterior and a posterior hepatic plexus. The fibers which go to the gallbladder form a small cystic plexus in the region of the cystic duct (fig. 4 7). The roots of the hepatic plexus arise from the right celiac ganglion and from the fibers which unite both celiac ganglions, from the aortic plexus and from the right renal plexus. The hepatic plexus sends branches to the liver, gallbladder, suprarenal glands, pyloric end of the stomach and head of the pancreas. We found no macroscopic ganglions in this plexus.

Raigorodsky differentiated four types of hepatic plexus after the four types of hepatic artery described by Rio-Branco.¹³ One of us (F. K.¹⁴) recently described twenty-four variations of the hepatic artery, and we were able to compare our nerve specimens with his original specimens. We found that several branches of the hepatic plexus always follow the abnormal branches of the hepatic artery. The main part of the plexus, however, is situated even in such cases on the anterior and posterior surfaces of the common duct and the portal vein.

The purpose of the following is merely to point out that certain clinical applications can be made of our anatomic observations. We mention some of them:

Relatively little damage is done to the important nerves in operations confined to the cystic duct.

In operations on the common bile duct, it is possible to damage important nerve fibers. It is true that in conditions involving the common duct, the pain is often pancreatic in origin. This need not,

13. Rio-Branco: *Essay sur l'anatomie et la médecine opératoire du tronc coeliaque*, Paris, 1912.

14. Kiss and Mihálik: *Ueber die Zusammensetzung der peripherischen Nerven und den Zusammenhang zwischen Morphologie und Funktion der peripherischen Nervenfasern*, *Ztschr. f. Anat. u. Entwgesch.* 88:112, 1928.

however, necessarily be so. If the same pain for which the patient was operated on persists, it is, of course, impossible to exclude with absolute certainty a pancreatic origin, even though the pancreas is clinically normal, particularly since the common bile duct is so closely related to the head of the pancreas. It is for this reason, too, that patients with conditions involving the common duct often complain of pain in the back. This pain can frequently not be differentiated from pancreatic pain or celiac neuralgia. That there should be pain in the back and vertebral tenderness is to be expected, since the gland, as well as important nerve fibers, lies retroperitoneally. Should, however, a new type of pain make its appearance after operation, one must always appreciate the possibility of some inflammatory or degenerative process involving the pain-bearing fibers which surround the common duct and should remember that this may be as frequent an occurrence as the ordinary scar formation in the common duct. The distribution of these fibers is such that an uncomplicated picture will only be present early in the cases, before there is an associated pancreatitis. Thus, in the more chronic cases, only a careful clinical history and tracing of the course and distribution of the pain will help to locate its original site.

Plexus Mesentericus Superior (figs. 1 23, 2 13 and 4 14).—This plexus forms a shell around the superior mesenteric artery. All the fibers arise from the celiac plexus (ganglions and linking fibers). The vast majority of the fibers run with the superior mesenteric artery to the intestines. Individual fibers run to the hepatic, cardiac, renal, pancreatic and duodenal plexuses.

Plexus Pancreaticus (figs. 1 21, 2 16, 3 10 and 4 11).—This rich plexus is not even mentioned in most textbooks and has never been illustrated. The plexus is made up of two parts. One part supplies the head of the pancreas, the other part the body of the pancreas. The part that supplies the head of the pancreas (figs. 2 16, 3 10 and 4 11) arises with many trunks from the celiac plexus (ganglions and connecting fibers) and from the superior mesenteric, aortic, hepatic and duodenal plexuses. The main part of the plexus lies behind the head of the pancreas and sends fibers from there into the head of the pancreas.

The other portion of the plexus, which goes to the body of the pancreas (fig. 1 21), arises from the splenic plexus, and its fibers enter, one after the other, the substance of the pancreas. Both portions are without macroscopic ganglions.

This distribution of nerves to the pancreas, through its substance and thence to the concavity of the duodenum, explains clearly why acute pancreatitis often simulates ileus and why the latter may be an associated observation. We have seen that in certain cases these nerves may be involved by scar, which may spread between the nerve fibers or even produce amputation neuromas. We suggest the foregoing possibilities

merely as some of the causes of pain in chronic pancreatitis. The celiac plexus may itself be involved by some inflammatory process or through pressure. The former also serves to explain certain types of pain that persist after operations on the biliary system. Pain in pancreatic conditions, particularly cysts, may be due to a "neuralgia" of the pancreatic and celiac plexuses. It may, on the other hand, be due to direct pressure



Fig. 5.—Hepatic, cardiac and duodenal plexus, anterior view. 1 indicates cardiac plexus; 2, caudate lobe of liver; 3, liver; 4, hepatic plexus; 5, right branch of hepatic artery; 6, gastroduodenal artery; 7 and 9, duodenal plexus; 8, duodenum; 10, stomach; 11, left gastric artery, and 12, pancreas.

on nerve endings rather than to pressure and pull on the intestine. Of pain that is pancreatic in origin, it can usually be said that the localization corresponds to the organ from which it emanated. The retroperitoneal position of the pancreas and of important nerve fibers explains, as we

have already mentioned, why there is pain in the back and why pancreatic pain is often increased when the patient is in the dorsal position. It seems that conditions of the pancreas limited to the head of the pancreas cause pain more frequently than those situated elsewhere in the pancreas. The relationship of the common bile duct and the presence of a separate plexus going to the head of the pancreas may perhaps explain this observation.

Plexus Duodenalis (figs. 2 14, 4 13 and 13a and 5 9).—This plexus is not mentioned or illustrated in atlases or textbooks. The plexus lies behind the pancreas on the posterior abdominal wall in the retroperitoneal tissue. The fibers arise from the pancreatic plexus and from the superior mesenteric plexus; a separate portion from the celiac plexus goes to the duodenal jejunal flexure. The branches reach the duodenum on its concavity. The plexus is without macroscopic ganglions. The distribution and arrangement of nerve fibers going to the duodenum suggest a route by which duodenal conditions may be reflected in the pancreas.

Plexus Mesentericus Inferior (fig. 1 10a).—This plexus arises from the aortic plexus and surrounds the artery that bears its name.

Plexus Spermaticus and Ovaricus (not illustrated).—The fine trunks of this plexus arise from the aortic and renal plexuses. The plexuses run with the similarly named artery.

THE MICROSCOPIC STRUCTURE OF THE CELIAC PLEXUS

The trunks of the splanchnic nerves and vagi bring three different morphologic kinds of fibers to the celiac plexus. The nonmedullated sympathetic fibers preponderate in the splanchnic nerves (fig. 6 2). Among these are mixed many thin medullated fibers (fig. 6 1) and also solitary, thick medullated fibers (fig. 6 4). In the abdominal part of the vagus, we found the same three kinds of fibers (fig. 7).

Kiss and Mihálik¹⁴ (1928) showed that the sensory and parasympathetic (vagus) fibers have thin medullary sheaths, that the motor fibers have thick medullary sheaths and that the sympathetic fibers are nonmedullated. These authors also found fibers with thick medullary sheaths in the posterior spinal roots, the function of which is unknown. On the basis of these and the aforementioned investigations, the thin medullated fibers in the splanchnic nerve are known to be sensory, whereas the thin medullated fibers in the vagus are parasympathetic, and the large solitary medullated fibers of the splanchnic nerves probably belong to those leaving the spinal cord through the posterior roots and probably conduct themselves centripetally. The most important fact which the surgeon has to know is that the sensory fibers to the celiac plexus run in the splanchnic nerves; that is why so many thin medullated

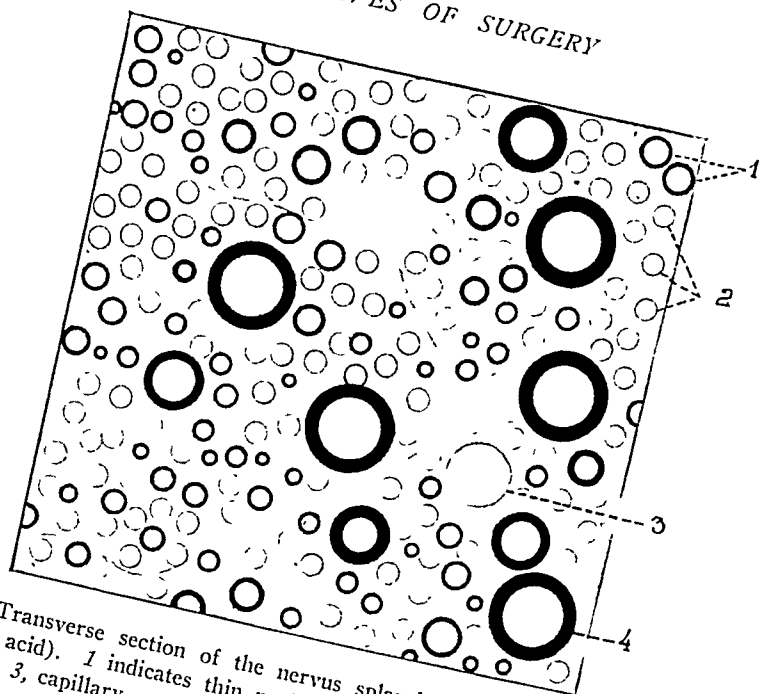


Fig. 6.—Transverse section of the nervus splanchnicus major sinister of an adult (osmic acid). 1 indicates thin medullated fibers; 2, unmyelinated (sympathetic) fibers; 3, capillary, and 4, thick medullated fibers.

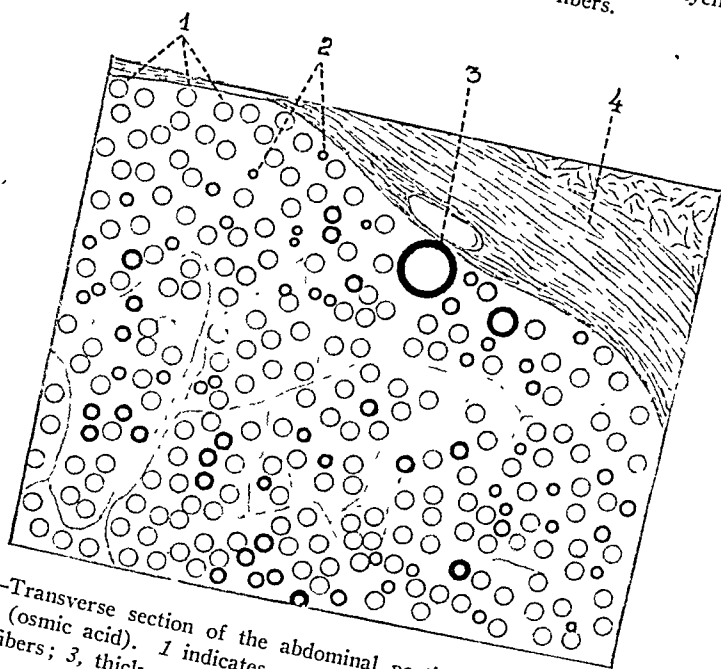


Fig. 7.—Transverse section of the abdominal portion of the left vagus nerve of an adult (osmic acid). 1 indicates unmyelinated (sympathetic) fibers; 2, thin medullated fibers; 3, thick medullated fibers, and 4, perineurium.

fibers are found in them. It follows from these observations that one finds in the branches of the celiac plexus the same three types of fibers that occur in the splanchnic nerves and in the vagi. In some plexuses, for example, the hepatic and renal plexuses, one finds fewer medullated fibers than one does in the branches of the superior and inferior mesenteric plexuses.

SUMMARY

A description of the celiac plexus from the standpoint of modern surgery is presented.

The celiac ganglions, the roots of the celiac ganglions, the branches of the celiac ganglions and the microscopic structure of the celiac plexus are discussed.

The plexuses of nerves going to the various abdominal organs are also mentioned. Particular attention is drawn to the descriptions and illustrations of the pancreatic and duodenal plexuses. These plexuses have never been illustrated before.

A block anesthesia of the splanchnic nerves gives the same results as infiltration of the celiac ganglions with their uniting branches.

In complete anesthesia of the splanchnic nerves or of the celiac plexus, the sensory, sympathetic and parasympathetic fibers are all blocked.

In order to obtain complete anesthesia, injections must be made on both sides of the splanchnic nerves, or in the celiac ganglions. A single injection suffices, because the splanchnic nerves, as well as the celiac ganglions, lie in loose retroperitoneal tissue.

We have drawn attention to the rich hepatic and pancreatic plexuses, which lie in the field of so many surgical procedures. Important fibers may thus be easily damaged.

It follows from the intimate relationship of the various plexuses with one another and with the centrally placed celiac plexus that certain lesions involving individual plexuses, such as the hepatic or the pancreatic plexus, may have their signs and symptoms reflected in other organs. Some disturbances referable to the duodenum and the pancreas after operations on the gallbladder may be explained on this basis.

THE BRANCHIAL APPARATUS

ITS EMBRYOLOGIC ORIGIN AND THE PATHOLOGIC CHANGES TO
WHICH IT GIVES RISE, WITH PRESENTATION OF A
FAMILIAL GROUP OF FISTULAS *

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Little has been written in this country concerning branchial cleft cysts and fistulas. Phases and fragments of the subject have been discussed in a few worthy papers. The interest aroused in a familial group of branchial fistulas recently studied in this hospital led us to feel that it would be worth while to present a fairly complete and comprehensive review of the whole subject in one paper.

Ninety case reports were studied, as well as the seventeen in our own archives. Many other case reports were not listed because of their incompleteness and because they presented nothing new.

Much of the information concerning the history of this subject was obtained from Wenglowski's extensive work.

HISTORY OF THE SUBJECT

The study of fistulas of the neck up to the presentation of von Ascherson in 1832 was in its infancy and in a chaotic state. After compiling his cases of lateral fistulas with all the known cases of fistulas and cysts at that time, von Ascherson concluded that these fistulas resulted from malformed branchial clefts which failed to close or to unite normally.

In view of the work of von Rathke, von Ascherson was cognizant of a prominent process that developed out of the second branchial arch in vertebrate embryos and that is the most prominent portion of the branchial apparatus; that is, the "Operculum branchiale of Rathke." Ascherson stated that the external orifices of fistulas pointed up under the operculum and thus the fistula was formed by a failure of the cleft boundaries to fuse or close. Succeeding authors, though they believed in the branchial cleft origin of the anomaly, opposed von Ascherson somewhat by introducing the conception that a fistula could develop from any of the four clefts. The fact that prompted this deduction was the

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variety of positions that the external orifice might and did take, being limited, as they knew, only by the region of the styloid process and sternoclavicular junction.

According to von Heusinger, the internal orifice of all fistulas was situated at the lateral wall of the pharynx at the base of the tongue. He also believed that the location of the external orifice determined which cleft was at fault, and stated that the fourth cleft was responsible in a case in which the orifice was at the sternoclavicular junction, because by dissection he had found that it coursed along the medial edge of the sternocleidomastoid muscle to the upper border of the larynx and then made a sharp turn toward the midline, opening at the root of the tongue.

Bland-Sutton and von Cussett devised schemas according to which one could determine from which of the four clefts a fistula developed. His doubted the truth and value of these schemas and maintained that the existence of a fistula pointing into the sinus praecervicalis but not into the pharynx is normal in the five weeks' embryo. Later the thymus develops from a portion of the sinus praecervicalis forming a connection between the two. If, he stated, the existing fistula does not grow downward in the thymus region but grows upward, then a true pathologic fistula exists. His, in 1889, changed his mind and stated that the thymus developed from the pharyngeal pouch and not from the precervical sinus.

Rabl refuted His, saying that the fourth cleft could not be a factor in the formation of fistula, because it is separated from the sinus praecervicalis by a thick mesodermal layer. The fistula could not result from the third because it is concerned with the formation of the thymus and therefore the fistula would have to be in close relation with the thymus, which is not true. He paid special attention to the origin of the viscera or organs of the neck from the second arch, since this arch is larger than the others. The second groove consists of a long irregular passage in which two rows of closely opposed epithelial cells divide the pharynx from the outside. He termed this the branchial canal and believed it to be the basis of the formation of fistula only, of course, when the epithelial membrane ruptures and therefore allows communication of the pharynx with the sinus praecervicalis.

In 1890, Kostaniecki and Milecki studied the literature in detail paying special attention to Rabl's work. They did not agree with the schemas of Heusinger, Bland-Sutton, etc., for the external opening of the fistula may at one time be high up near the jaw, then may close and open later in a lower position, and they therefore thought it foolish to say that the position of this opening had such significance as was claimed. The inner opening into the pharynx, however, is constant for any particular cleft or groove. The most frequent and constant internal opening is located in the suprathonsillar fossa, and they concluded from a search of the literature that this corresponded with the second arch.

thus agreeing with Rabl. According to these two men, no branchial cleft could persist in toto, nor could in itself be the cause of a fistula. In the case of the complete fistula, the limiting membrane must be ruptured, and in this way the pharyngeal pouch must first break into the cervical sinus. Thus the complete fistula originates from a rupture of the second pharyngeal pouch into the cervical sinus.

Although later work was based on the observations of these authors, yet some persisted in believing that the first, third or fourth grooves were occasionally the origin of cysts and fistulas. Kostaniecki and Milecki believed that Virchow's case in 1865 originated from the first because of certain coexisting anomalies of the ear.

They, however, denied the validity of Watson's argument concerning a case in which the fistula followed the course of and ran in the stylopharyngeus muscles. That is, he concluded that since the stylopharyngeus muscle originates from the third arch, the fistula must have originated from the third cleft. The refutation was based on the fact that the musculature develops at too late a period to be of significance in this way.

Wenglowski held that if the lateral fistulas belong to the second groove, then the inner openings must be within the limits of this groove or cleft, that is, the arcus palatoglossus muscle (anterior border) and the arcus palatopharyngeus (posterior border). Never, he added, has an inner opening of a fistula been found within the tonsil or between the two limits mentioned. In the cases of Kostaniecki and Milecki, Koztowski, Kotalicki, Neuhöfer, Mobitz, Watson, Rehn, etc., the inner opening pointed at the root of the tongue (unterhalb) in the tonsil fossa and behind the arcus palatoglossus. The inner openings of the lateral fistulas, therefore, since the arcus palatoglossus is formed by a deeply embedded muscle belonging to the third arch, are closely related with the third and not the second arch.

Kostaniecki and Milecki and their advocates argued that the outer opening may be found anywhere and was of no import as regards the origin of the fistula—that the outer opening developed from the inflammation, suppuration and consequent rupture of the inflammatory mass, and the rupture might be at any height or position, depending on the depth or extension of the suppurating cyst or fistula.

Again, to the contrary, Wenglowski stated that after studying a series of cases, one becomes cognizant of the fact that the external openings point in a definite place as a rule. That is, they occur along a line extending from the angle of the mandible to the middle of the sternum, along the medial border of the sternocleidomastoid muscle. If suppuration and inflammation were factors in determining the orifice, it would be only logical to expect it to point anywhere and not follow a definite course as we know it does. That is, they could open lateral to the sternocleidomastoid muscle into it or even into the pharynx and esopha-

gus. In further opposition to Kostaniecki and Milecki, Wenglowski contended that the branchial apparatus does not spread itself into the viscera of the neck but belongs to the head. The second, third and fourth branchial arches do not extend downward but backward or posteriorly. It is self-evident that the branchial arches, as well as the grooves, are definitely and precisely fixed anatomically and topographically. If the formation of the fistula were due to the branchial clefts remaining open, then the fistula would have to open in the region of the submaxillary angle and there would be no basis for its opening lower in the neck. Then again some cases are found in which the external opening is located at the medial edge of the sternocleidomastoid muscle and in exploring the canal one finds that it does not lead upward but downward to the sternum, where it ends blindly. These cases, he contended, cannot have any connection with the branchial apparatus.

History with Special Reference to the Development of the Branchial Apparatus.—The first accurate embryologic description of the branchial apparatus in vertebrates was given by Rathke, in 1825. He described the arches and clefts in the three weeks' embryo of a pig and compared them with the branchial apparatus of the shark.

In 1827, von Baer described four clefts in the human embryo.

In 1832, von Ascherson for the first time discussed the origin of fistulas of the neck from the branchial apparatus, while in 1877, von Cusset made a compilation of various pathologic conditions of the neck independent of the branchial apparatus. He claimed that in man the first arch develops on the fifteenth day and the fourth during the first half of the second month. All arches extend to fuse with their fellows of the opposite side. Their substance consists of embryonic tissue lined externally with flat and internally with cylindrical epithelium. All arches arise in the region of the base of the skull, but because of the rapid growth of the first the lower four are crowded caudally. The rims or borders of all four grooves or furrows are definitely delineated at first but soon fuse, and fuse on the outside first because they grow more rapidly here. If the epithelium does not disappear before this fusion, many pathologic conditions result. The opposing surfaces of all the clefts fuse before the end of two months.

In 1881, His, studying exclusively human embryos and applying the reconstruction method, changed considerably the study of embryology. He found that the endodermal and ectodermal layers came in close apposition with at least only a very small amount of mesoderm or partition between the pharynx and the outside in the region of the clefts. It is not risking too much, he stated, to suppose that this membrane might tear, though, of course, this is not the rule. As one goes caudalward, the distance between the anterior ends of the arches becomes greater

so that at one time a triangular area is formed with its apex upward and was termed by His the mesobranchial field. During further growth, the arches telescope themselves from above down so that looking from the outside, the fourth is covered by the third and the third by the second. In this way, the third and fourth become encased in a cavity in the wall of the neck by the down growth of the second arch. This cavity His called the precervical sinus.

Von Mall (1887) agreed with His and Born. He found that in birds and higher vertebrates no breaking through of the branchial clefts took place, and that these clefts are always separated by a membrane composed of two epithelial layers. In view of the fact that these membranes are thin and delicate, it is possible, he stated, that they could rupture in the living embryo and thus give rise to many anomalies.

In 1888, Piersol came forth with his study of rabbit embryos. He came to the conclusion that the inner pharyngeal pouches are developed earlier and mature later than the outer arches and clefts. In mammals, the rule is, according to him, that the branchial clefts and pharyngeal pouches are separated by limiting membranes and that a tear can take place only in the second. In the first three pharyngeal pouches, two parts can be distinguished, the ventral horn and the posterior extremity, while, in the fourth, the parts cannot be differentiated. Out of the ventral horns, with the exception of the first, the tubular epithelial formations grow.

Foll, von Liessner, Kotschenke, Zimmerman, etc., took a stand opposite to that of His.

In 1884, Foll stated, after studying a 5-6 mm. human embryo, that the branchial clefts must be considered as continuous structures, even though delicate limiting membranes are interposed.

In 1889, von Liessner (studying chick and sheep embryos), concluded that patency of the branchial clefts does exist in all animals with certainty.

Hammer stated that in the 5 mm. embryo, the pharyngeal pouches are well developed and the second is perforated bilaterally at its base.

In summary, therefore, the prevailing theories concerning the origin of the so-called anomalies of the branchial cleft are:

1. The branchial clefts are responsible for cysts and fistulas. (a) A fistulous opening or rest may persist from any of the four clefts (von Heusinger, Bland-Sutton, von Cusset, His, etc.). (b) Only the second cleft can be at fault (Rabl, etc.). (c) The cervical sinus is responsible for the external aspect of the anomaly (von Ascherson, Kostaniecki, Milecki, His, etc.).

2. The thymic stalk and not only the clefts is responsible for their origin (Wenglowski).

EMBRYOLOGY

Early in the life of the embryo (within the first three weeks of intra-uterine life), five bars are prominent in the region of the neck (figs. 1 and 2). These bars are spoken of as branchial arches and the depressions or slits between them as branchial grooves. Within the pharynx (fig. 3) there is a bar and groove opposite each external bar and groove. These structures are covered by ectoderm externally, endoderm internally and contain mesoderm between the two. The mesoderm between the external and internal grooves is absent or nearly so, so that the ectoderm and entoderm are practically adjacent, the membrane so formed

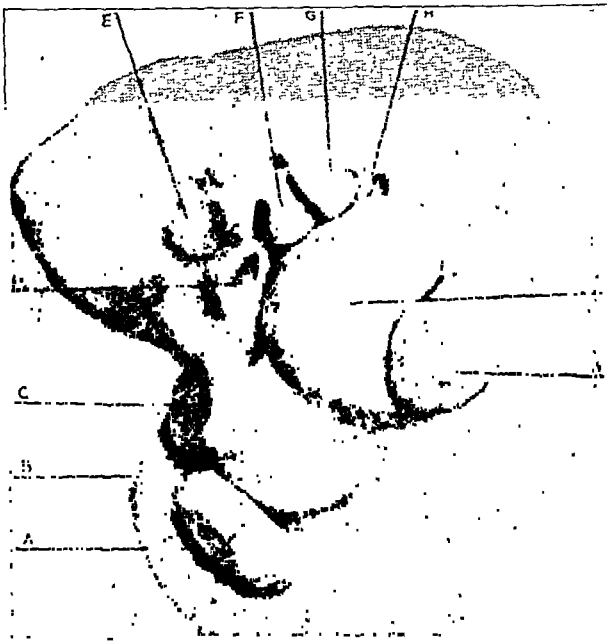


Fig. 1.—A 6.5 mm. embryo. *A* indicates lower extremity, *B* the tail, *C* the umbilical stalk, *D* the nose, *E* the eye, *F* the lower portion of the first branchial arch, *G* the second arch, *H* the third arch, *I* the heart and *K* the upper extremity. (From Wengłowski.)

in the first groove persisting to give rise to the tympanic membrane. These branchial arches and grooves are the forerunners of the gill bars and gill slits, respectively, in fishes, the adjacent ectoderm and entoderm in the depths of the groove having been absorbed to allow the pharynx to communicate with the outside. Hence the derivation of the word branchial (*βραγχια*; gills), meaning pertaining to or resembling the gills of a fish. In mammals, the branchial bars are the anlagen of definite and important structures of the face and neck. Though the grooves normally disappear, except the first, which becomes the external auditory

meatus and eustachian canal, they, by their embryologic nature, not altogether uncommonly persist by failure to occlude or by inclusion of epithelial and endothelial remnants and lay the foundation of the most interesting curiosities and pathologic problems that one encounters in the neck. It is, of course, with the latter that one wishes ultimately to deal, but they are often so complex that some knowledge of their embryologic development and relations is indispensable if one is to have accurate judgment in diagnosis and assurance in treatment.



Fig. 2.—A 6.5 mm. embryo. *A* indicates the branchial groove, *B* the mandibular portion of the first arch, *C* and *D* the nasofrontal process, *E* the eye, *F* the maxillary division of the second arch, *G* the second arch (operculum) and *H* the third arch (operculum). (From Wengłowski.)

The Arches.—The first arch is larger and grows more rapidly than the others, greatly deepening the oral fossa. It early divides into two portions. An upper, the maxillary, portion gives rise to the upper jaw, the lateral parts of the upper lip and the cheeks. The lower portion gives rise to the lower jaw, lower lip and region of the chin. This arch, as do the remaining arches, contains a rod of cartilage, which in this particular arch is known as Meckel's cartilage (figs. 3 and 7). This

cartilage extends from the symphysis menti to the tympanic cavity and lays the foundation of that part of the mandible which develops as intra-cartilaginous bone and which carries the incisor teeth (the remainder being intramembranous bone), the sphenomandibular ligament and two ossicles (malleus and incus).

Both ends of the rod of cartilage in the second arch ossify, the anterior end becoming the lesser cornu of the hyoid bone and the posterior end the styloid process, which fuses with the temporal bone. The intervening portion persists as the stylohyoid ligament.

That portion of the stapes other than the base is probably derived from a portion of the cartilage of the second arch, though its base develops as intramembranous bone. The portion of cartilage in the third arch becomes the greater horn of the hyoid bone, that from the two

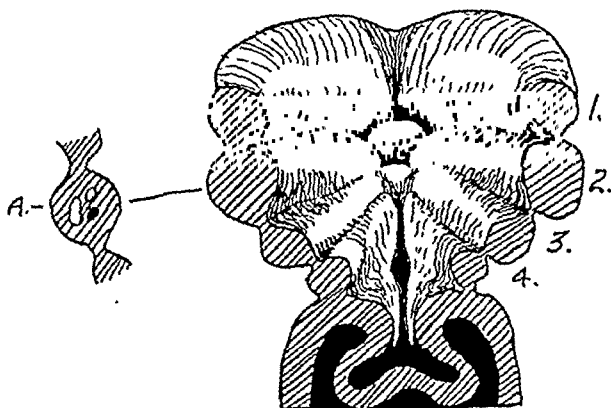


Fig. 3.—A diagram to illustrate the branchial arches and grooves. *A* shows the cartilage, artery and nerve contained in the arch.

sides fusing through the body, which also develops from the third arch, and the whole fusing with the lesser cornua, later to form one piece.

The cartilage in the anterior portions of the fourth and fifth arches goes to make up the skeletal elements of the larynx and though it is thought that the greater part, at least, of the thyroid cartilage is developed from the fourth arch, the derivation of the remaining structures is not certain.

In addition to the structures mentioned, which are derived from the cartilage bars of the arches, one must consider the vascular, nervous and muscular content and also the epithelial bodies of the neck to which the arches give origin.

Vascular Content: One recalls that in the human embryo, six aortic arches appear on either side of the pharynx (fig. 4), taking their origin from the ventral aortic trunk and roots, coursing through the branchial arches and joining posteriorly the dorsal aortic roots. In the fishes and

larval amphibians, in which the arches and grooves develop into the gill bars and clefts, these aortic arches persist and develop into a ramifying network of small capillaries in the gill bars, which, when bathed by water circulating through the clefts, absorb its dissolved oxygen.

In mammals, however, marked changes occur early in embryonic life. The first two arches disappear completely (fig. 5), though the origin of the facial artery marks the anterior end of the first arch and the origin of the lingual marks the anterior end of the second. The third becomes the proximal portion of the internal carotid, the distal portion of the internal carotid being the cephalic remainder of the dorsal

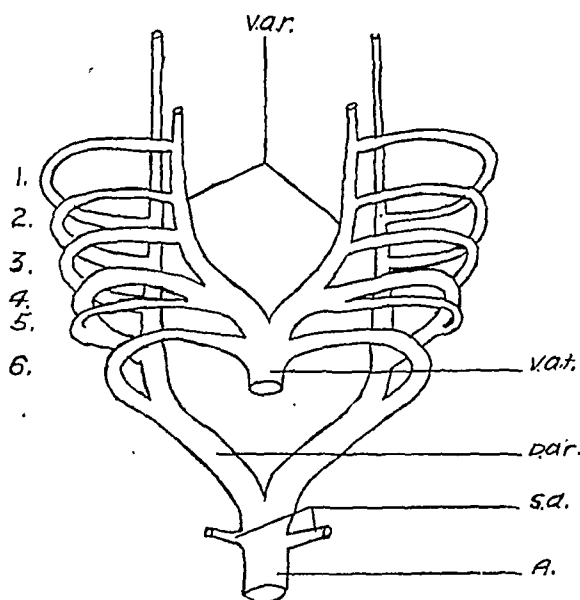


Fig. 4.—A diagram of the aortic arches of a mammal. *var* indicates the ventral aortic roots, *vat* the ventral aortic trunk, *dar* the dorsal aortic roots, *sa* the subclavian arteries and *A* the aorta. (From Bailey and Miller.)

aortic root from the junction of the third arch on. The fourth arch on the right and part of that dorsal aortic root becomes the right subclavian, while on the left the fourth arch remains as the arch of the aorta. The fifth and sixth arches disappear, with the reservation that the sixth on the left leading from the pulmonary artery (which has now been separated from the ventral aortic trunk by the septum aorticum) to the descending aorta persists for awhile as the ductus arteriosus (Botalli) and is the future ligamentum arteriosum. We will only mention here and refer to the fact in more detail later that a persistent second groove or remnant of the same would have to course superior to the internal

carotid and that from a third groove would have to course inferior to that artery. It is a well known fact that those fistulas the internal orifices of which are in the suprtonsillar fossa and many branchial cysts lie in the fork of the internal and external carotids.

Nervous Content: The nerve of the first arch is the third division of the fifth (mandibular), while the second contains two, the facial (seventh) and the auditory (eighth). The third arch contains the glossopharyngeal (ninth), the fourth arch the superior laryngeal branch of the vagus and the fifth the inferior laryngeal.

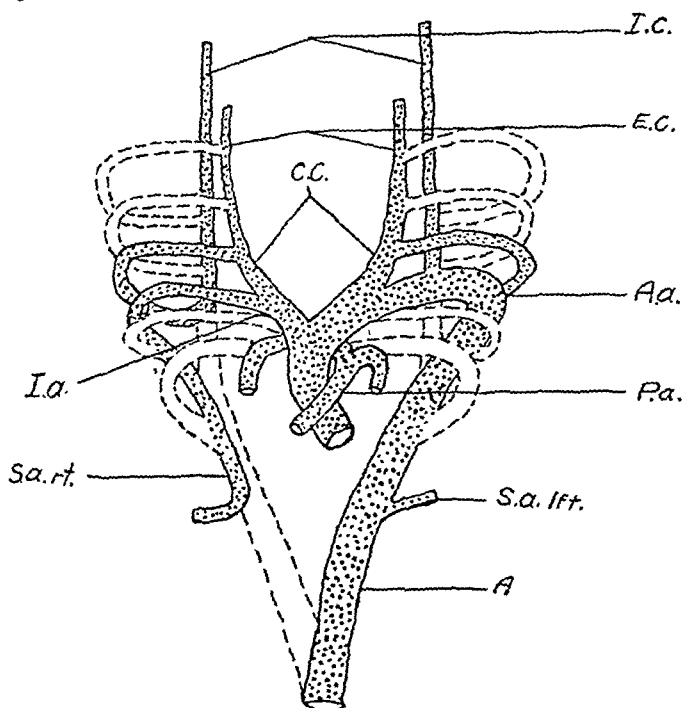


Fig. 5.—A diagram representing the changes in the aortic arches of a mammal. *I C* indicates the internal carotids, *E C* the external carotids, *C C* the common carotids, *I a* the innominate artery, *A a* the aortic arch, *P a* the pulmonary artery, *S a rt* the right subclavian, *S a lft* the left subclavian and *A* the aorta. (From Bailey and Miller.)

It is interesting to note in passing that, since the recurrent laryngeal is laid down anterior to the fourth arch, its forced migration caudalward by the subclavian on the right and the arch of the aorta on the left is accounted for.

Muscular Content: In view of the extensive and remote migration of the muscles about the face and neck, the problem of deducing their exact origin would be complex were it not for the fact that the nerves they carry with them serve as a key. Therefore, the muscles derived from the first arch (i.e., those innervated by the mandibular nerve) are

the muscles of mastication, the mylohyoid, anterior belly of the digastric, the tensor palati and tensor tympani. Those from the second arch (facial) are the stapedius, stylohyoid, posterior belly of the digastric, the platysma myoides and all the muscles of facial expression. Those of the third arch (ninth) are the stylopharyngeus and some of the soft palate muscles. The fourth (superior laryngeal) gives rise to some of the soft palate muscles, the constrictors of the pharynx and the cricothyroid, while the fifth (inferior laryngeal) is the origin of the intrinsic muscles of the larynx.

From the foregoing considerations one is able, if one assumes that either the second, third or fourth groove persists, to deduce the theoretical course of such a resulting fistula or cyst developing from the included rests. In the case of the second, it should pass between the external and internal carotid arteries and superior to the ninth nerve. The third should pass inferior to the internal carotid, lateral to the common carotid, inferior to the ninth and superior to the superior laryn-

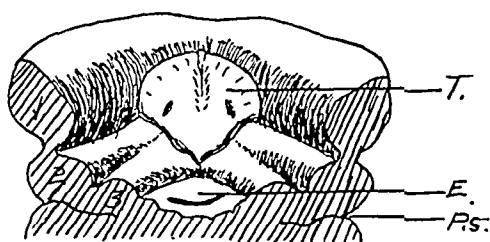


Fig. 6.—A diagram to illustrate the enclosure of the precervical sinus (*P S*). *T* indicates the tuberculum impar and *E* the epiglottis.

geal nerves. The fourth should course below the subclavian nerve on the right and the arch of the aorta on the left.

As a matter of fact, the situation is not quite this simple, for at about the fourth week of intra-uterine life the second arch grows outward and downward to meet the body wall, thereby enclosing the external aspect of the second, third and fourth grooves (fig. 6). The ectoderm lined pocket so formed is known as the cervical sinus and is probably responsible in diverse ways for the congenital anomalies. Thus, any of the following mechanisms might possibly obtain: 1. Any one of the grooves might remain as a fistula or a tract of included ectoderm and entoderm in pure form, having its origin and termination in its own normal embryologic location. 2. Any one of the grooves might persist with its normal embryologic origin on the pharyngeal side and by continuation in the cervical sinus have its external opening anywhere from the tip of the styloid process to the sternoclavicular joint. This might explain the fact that the internal orifice of a branchial fistula is almost always in the supratonsillar fossa (and, as will be seen later, undoubtedly originates

in the second groove), though its external orifice varies between the limits described. 3. Any groove might persist in whole or in part and connect with another groove through the cervical sinus.

Epithelial Bodies Derived from the Arches.—Tonsils: The tonsils (third month) arise in the region of the ventral part of the second inner branchial groove, are therefore entodermal in origin and grow as hollow buds into the mesenchymal tissue. Hollowed buds join the main bud, lymphoid cells wander in and by the third month after birth distinct lymph follicles with germinal centers are present.

Thymus: From the ventral part of the third branchial groove on each side (in the 6 mm. embryo), an entodermal evagination appears.

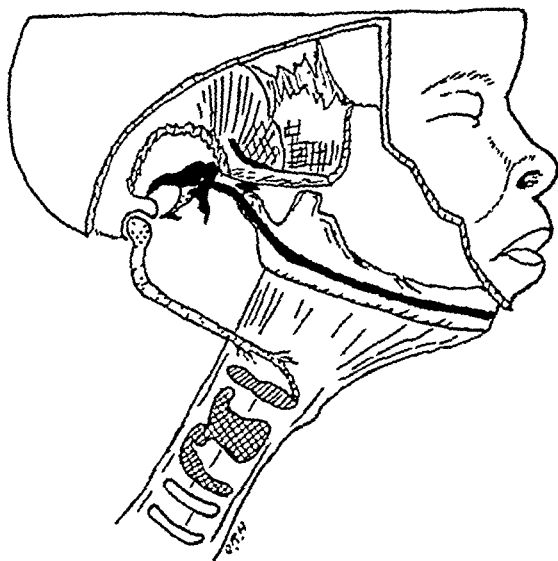


Fig. 7.—A diagram to illustrate the derivatives of the branchial arches. Complete black indicates the first arch (Meckel's cartilage), stipple the second arch, single cross hatch the third arch and double cross hatch the fourth and fifth arches.

This soon severs connection with its parent epithelium and grows caudalward as the thymic stalk, being ventral to the carotid arteries in the 16 mm. embryo and resting on the cephalic surface of the pericardium in the 29 mm. embryo, in which further differentiation of the bilobed thymus is carried out (fig. 8).

Thyroid Gland: In the 3-5 mm. embryo, at the point where the tuberculum impar and the two paired anlagen of the tongue join, there occurs an evagination of pharyngeal entoderm. From this, the site of the future foramen-caecum linguae, the mass of epithelium grows caudalward along the ventral surface of the larynx, giving rise to the thyroid duct. The terminal portion enlarges into the two lateral lobes remaining

connected by the isthmus, while the pyramidal process is a secondary growth from the isthmus, lateral lobes or distal thyroglossal duct.

CLASSIFICATION

It is obvious at once that branchial cysts may be classified from several points of view.

As to Position.—1. Branchial cysts may be superficial or deep (Bailey's classification). 2. They may be auricular or auditory, parotid, submaxillary, sublingual, pharyngeal or tracheal. This classification as to anatomic position alone not only is insufficient but fails to indicate the origin of the cyst, which is important.

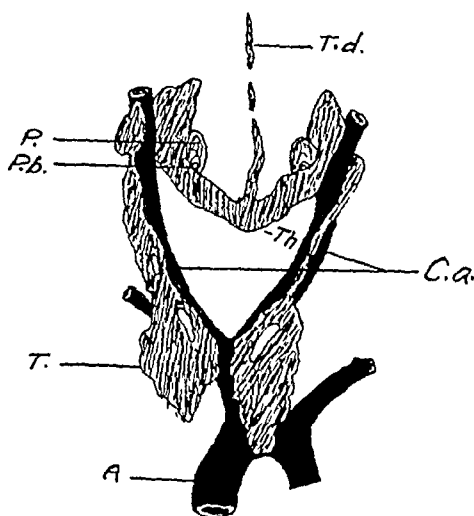


Fig. 8.—A diagram showing the branchial derivatives of a rabbit embryo of 16 mm. *T d* indicates the thyroglossal duct, *P* the parathyroids, *P b* the post-branchial bodies, *Th* the thyroid, *C a* the carotid arteries, *T* the thymus and *A* the aorta. (From Bailey and Miller.)

As to Cleft Giving Origin.—This classification is of little value, for it is a greatly disputed point whether more than one cleft is ever responsible for these congenital anomalies. Furthermore, in the case of cysts, it is often difficult to know which groove was responsible for its origin.

As to Contents.—1. Some branchial cysts are mucous cysts. These are usually the deep ones, lined by entodermal epithelium. Many of the so-called ranular cysts belong to this group, including the hour glass cyst of Roser and the congenital mucous cyst in the region of the base of the tongue and the sides of the larynx. 2. Some branchial cysts are atheromatous. These, at first having the appearance of dermoid cysts, are found to contain grumous material, which is entirely desquamated

epithelium without the elements of further differentiation, that is, hair, sweat glands, etc. 3. Other branchial cysts are serous. These have been known as "hydrocele colli" (Mannoir), "congenital hygroma of the neck" (Wernher), "congenital hydrocele of the neck" and "congenital cystic tumor of the neck" (Thomas Smith). These tumors appear as simple cysts lined with pavement epithelium and contain a limpid watery or tenacious fluid holding in suspension epithelial cells and cholesterol crystals.

Hematocysts of Branchial Clefts.—Of these there are two kinds: (1) those which are in communication with vessels and which can be emptied by pressure, and (2) those which are truly simple serous cysts with an admixture of blood, probably from minute hemorrhages in the wall of the cyst. These have been termed "haematocele colli" by Michaux. Senn mentioned that there might also be a true venous cyst in this location resulting from either a segment of vein completely constricted off at both ends or a saccular dilatation which has been constricted at its neck. Such a cyst, though in the region of the saphenous vein, was described by Paget in 1853.

Type of Lining Epithelium.—Lastly, branchial cysts may be classified according to the type of epithelium lining the wall and hence would resolve themselves into: (1) branchial cleft cysts with cylindrical epithelium, or branchial cleft mucous cysts; (2) branchial cleft cysts with pavement epithelium, or branchial cleft epidermoid cysts.

It seems that the latter classification by taking into full account their origin is by far the better.

FAMILIAL AND HEREDITARY TENDENCY

Though there are no reports on which to base an assertion of a hereditary tendency to branchial cysts, there have been several instances of such a tendency to fistulas. The following are reported in Virchow's archives (1861): mother and eight children; mother and son in three instances; mother and daughter; two sisters, a brother and a maternal grandmother; aunts in two instances.

In the familial instance we are reporting, a mother and three of her five children presented fistulas, but she is aware of no similar defect in other members of her family. Thus far, therefore, branchial fistulas may be familial and hereditary, and seem to be inherited only from the mother. No instances, so far as we know, have been reported of inheritance from the father.

CLINICAL FEATURES

This description of the clinical facts was drawn from a study of ninety cases taken from the literature and eighteen additional cases taken

from the archives of this hospital. An outline of the main facts brought out in these case reports is given at the end.

Cysts.—The average age of the persons in whom the ninety cases occurred was about 21 years; the oldest was 48 and the youngest 3 weeks at the time the patients were seen in the clinic. If, however, the average duration of the development of the cyst, which is about four years, is subtracted from these ages, the average age at onset of the cyst is 17 years. This applies only to those appearing some time after birth. In nine patients of this series (21 per cent), the cyst was present at birth. Though fistulas are not infrequently bilateral, we have found no report of a bilateral branchial cyst.

The patient comes to the clinic usually because of a painless swelling in the neck. Owing to its painless nature, the cyst often reaches the size of a hen's egg or lemon before it seriously attracts the patient's attention. In a small percentage of cases, however, the patient complains of pain (as in Thomson's¹ case, no. 29 in the accompanying table), particularly when the cyst swells and becomes tense. In respect to the swelling, many of the patients give a history of fluctuation in size. The cyst is often noted as becoming larger and more tense during the process of salivation, and indeed, as will be referred to later, Coplin² stated that in the case of branchial fistulas, stimulation of salivary secretion by citric acid or mastication usually stimulates secretion from the sinus even when it does not communicate with the alimentary canal. Though the cyst most frequently has an inconspicuous and insidious beginning, occasionally the patient traces it to some shock or injury, as in Jefferson's³ case (no. 9) and as in Glover's⁴ case (no. 27) of a patient who traced a slight swelling on the left side of the neck to an injury received while lifting heavy pipe in the oil fields. There was pain in his neck and it was stiff and sore for several days. He thought he had ruptured a muscle.

Though it is more frequent for the incomplete fistulas opening internally to give their first trouble after tonsillectomy, yet occasionally a deep cyst opening through a fistula internally will be brought to light through inflammation, suppuration or continued drainage after a tonsillectomy (Johnson,⁵ case 3). Not infrequently does a cyst in conjunction with a fistula opening either externally or internally break through and drain copiously from time to time, obviously being of considerable annoyance. In one instance, the material issuing from an inner orifice was of foul

1. Thomson, J. W.: A Case of Branchial Cyst, *Lancet* **212**:76, 1927.

2. Coplin, W. M. L.: Branchial Cysts and Fistula, *Proc. Path. Soc. Philadelphia* **4**:109, 1900.

3. Jefferson, J. C.: Abnormalities of Branchial Origin, *Clin. J.* **45**:424, 1916.

4. Glover, G. E.: Branchial Cyst, *M. Rec. & Ann. San Antonio* **16**:171, 1922.

5. Johnson, J. A.: Branchial Cysts and Fistulae, *Minnesota Med.* **9**:514, 1926.

odor. Altogether too frequently to speak well of diagnostic acumen, the patient relates that the swelling has been aspirated many times (from four to fifteen times),⁶ and occasionally incised and drained only to have it return again in every case. Such a procedure always sooner or later introduces infection. With the varying degrees of subsequent reaction, from mild inflammation to suppuration, the latter frequently with poor drainage, the lesion gives rise to pain and establishes a focus of pus and of toxins, which debilitate the victim greatly and cause a loss in weight. The inflammation also renders the wall of the cyst adherent to the surrounding structures, so that any subsequent attempt at dissection is made extremely difficult (Seed,⁷ case 30). Not infrequently symptoms of pressure on contiguous structures are manifested. For example, Thomson¹ reported a case of cyst (no. 29 in the table), which swelled periodically and was associated with pain in the shoulder, dysphagia, dyspnea and a husky voice, which later advanced to complete aphonia, with fixation of the left vocal cord. These symptoms completely disappeared after extirpation of the cyst.

Though we are now discussing cysts, it is interesting to note Carp's⁸ case of fistula (no. 8) in a boy of 5, who was troubled for two years by a dry, hacking cough, worse at night and when the fistula did not discharge. At operation, the fistulous tract was found to be adherent for a short distance to the vagus. The paroxysms of coughing completely disappeared after the operation. In Smith's⁹ case (no. 43) of fistula in a child of three weeks, respiration and deglutition were markedly impaired. In one of our cases (E. E.), the fistula on the left opened into a cyst the size of which varied from that of a filbert to that of a hen's egg, and the patient would experience, in association with the swelling, nervousness, restlessness, hoarseness and palpitation of the heart. During the first attempt to probe the complete fistula on the right, it seemed that when a certain point was reached and before the probe was through the inner orifice, coughing, uneasiness and distress were stimulated. On the second attempt to probe the tract, sometime later, when we were unsuccessful on account of partial obliteration, the mere introduction of the filiform caused vomitus to well up in the throat.

The right side of the neck was involved in seventeen (35.5 per cent) and the left in twenty-one (64.5 per cent) of the cases. This proportion is about equally true for male and female taken separately.

6. Bailey, H.: The Clinical Aspects of Branchial Cysts, *Brit. J. Surg.* **10**: 565, 1922-1923.

7. Seed, L.: Branchial Cyst, *S. Clin. N. America* **6**:1029, 1926.

8. Carp, Louis: Branchial Fistula; Its Clinical Relation to Irritation of the Vagus, *Surg. Gynec.* **42**:772, 1926.

9. Smith, Thomas: Congenital Cystic Tumor, *St. Bartholomew's Hosp. Rep.* **2**:16, 1866.

On examination, one finds a regular hemispherical tumor, the skin surface over which appears smooth. The size may be from that which is just detectable to that which fills the whole side of the neck. It is often described as being the size of a filbert, a walnut, a hen's egg or an orange, etc. It may be large enough to protrude in the floor of the mouth as in the case reported by Senn¹⁰ (no. 40). Treves¹¹ reported a case in an infant (no. 44), in which the whole side of the neck and the thorax on that side down to the umbilicus was involved. The cyst may be located about the pinna and anywhere from this region to the junction of the sternocleidomastoid and the clavicle, and even may extend somewhat lower than this, so that it is partly substernal, the swelling pointing in the suprasternal notch. Those cysts that are located in the neck bear a definite and constant relation to the sternocleidomastoid muscle. It can be said with impunity that if they are of any considerable size, they extend, at least in part, under this muscle and this is one of the most dependable clinical features of this type of cyst. Submaxillary cysts are, of course, excepted. Frequently the fibers of the muscle will be thinned out owing to long continued pressure from the cyst and one might get the false impression that the muscle belly goes through the tumor. The true relationship in many cases, however, may be easily brought out by merely having the patient attempt to rotate his head while the examiner holds the chin, so as to place the sternocleidomastoid muscle on the stretch, and at the same time palpating it. As the cysts grow larger to accommodate their accumulated secretion and contents, they dissect their way, of course, along the planes of least resistance and the direction that they take depends considerably on the depth of the cyst. In regard to their depth, Bailey⁶ has classified them as (1) those lying just beneath the skin; (2) those extending deeper and attached to the internal jugular; (3) those passing between and straddling the bifurcation of the common carotid, and (4) those of the mucous or columnar cell type lying entirely posterior to the common carotid next to the pharynx. The larger and more superficial ones may extend toward the midline and bring up the question of thyroglossal duct cyst, but they practically always are eccentric enough to preclude being the latter. It seems to have been the rule that the cysts taking origin in the neck may dissect as high as possible under the sternomastoid muscle and therefore behind the ear but seldom dissect over the jaw and anterior to the ear as may hygromas. This point was brought to bear in a recent questionable diagnosis at this hospital.

10. Senn, N.: Branchial Cysts of the Neck, *J. A. M. A.* **3**:197 (Aug. 23) 1884.

11. Dissection of a Congenital Hydrocele of the Neck, *Virchows u. Hirsche Jahresbericht* **1**:280, 1882; quoted by Pranesk.

The uncomplicated cyst is most frequently obviously fluctuant and rather soft, though the so-called atheromatous or dermoid types may be rather firm and nonfluctuant. The latter may be lobulated, rendering their differentiation in diagnosis from tuberculous glands especially difficult. This difficulty is increased if secondary infection has taken place and more especially if there is an externally opening fistula through which the puslike or grumous material periodically escapes. If the latter condition is present, an examination of the fistulous orifice with a hand lens will be enlightening, provided the inflammatory process has not completely destroyed the anatomic definitive. The uncomplicated cyst has been described as having a multilocular feel, but this is not common. Although one cannot get the sensation by feeling through the overlying structure, yet, at operation, when feeling through only the thin wall of the cyst, the sensation one gets is much like that when feeling lung. The cyst wall is not adherent to the overlying structures, but feels to be so deeply, and this assumption is, in most cases, proved to be true at operation. Uncomplicated branchial cysts are not painful, except in rare cases owing to pressure, and are not tender.

Secondary infection, of course, changes the picture completely. All the signs of inflammation obtain, with adherence to the surrounding structures, pain, tenderness, fever, leukocytosis, etc.

Fistula.—In the series of sixty-two cases of branchial fistulas, 53 per cent occurred in females and 47 per cent in males. Fifty-one and eight tenths per cent were on the right side, 31.4 per cent were on the left and 16.8 per cent were bilateral. One interesting case reported in Virchow's archives (1861) presented multiple small openings on the right at the junction of the sternocleidomastoid muscle with the clavicle. This is the only case of multiple unilateral fistulas that we were able to find record of. It may be noted that the right and left incidence here is the reverse of that for cysts.

In the case of fistula, the feature that brings the patient to the hospital is practically always drainage, which may be periodic. It may consist of clear, tenacious mucus (said not to be of the chemical character of saliva) or thin, milky and puslike.

True fistulas practically always exist from birth and may be of such capillary dimensions as often to escape notice. Obviously, the incomplete fistulas that open only internally may never come to attention unless they are large enough to fill with food or unless they become infected and drain habitually, a condition which, as mentioned, is not infrequently initiated by tonsillectomy. A fistula opening into the trachea may give rise to air sacs and present the features of what has been termed "aerial goiter," "aerial bronchocele," "tracheocele" and "hernia of the trachea" (Coplin; ² Eldridge ¹²). Eldridge described such

12. Eldridge, S.: Am. J. M. Sc. 78:70, 1879.

a condition in a patient 26 years of age—an air cyst on each side of the lower part of the pharynx and the upper part of the trachea, which grew larger on expiration and increased the circumference of the neck from 40.5 to 49 cm. The external orifice may be situated about the pinna, or in the neck always just anterior to the sternomastoid muscle.

Often there is a small areola of brownish discoloration about the external orifice and occasionally a small bit of tissue, which is invariably found to contain a piece of cartilage. These are known as "super-numerary" or "cervical auricles."

By picking up the skin about the orifice, one can feel the cordlike tract extending into the neck. By traction, it prevents the orifice from being lifted as high as the surrounding skin.

Mention has been made of such symptoms and signs as pallor, uneasiness, palpitation of the heart, coughing and vomiting on probing the fistula, which can be adequately accounted for by the proximity of a portion of the tract to the vagus.

Among unusual cases that have been reported, the following are of passing interest:

Lesser reported a patient in 1840 (Virchow's archives), who traveled with a show and made his livelihood by passing a curved knitting needle into the pharyngeal orifice of a fistula and extracting it from the external orifice.

Ascherson presented a patient who, though having originally only one external orifice, later developed three, the fistula closing and opening in a new place each time.

Von Berg showed a patient in whom the external opening was in the incisura thyroidea and communicated with the middle ear. When the external orifice closed, material would discharge from the ear, while injections made in the external opening gave rise to pain in the middle ear.

Branchial cleft fistulas have also been described as occurring in cats and dogs.¹³

DIAGNOSIS

In arriving at a diagnosis of branchial cleft cyst, one should have in mind that it is usually a uniform, painless, fluctuant, semifixed, non-translucent tumor with a characteristic relationship to the sternocleidomastoid muscle and without tenderness. The differential diagnosis involves the following:

Adenitis.—Nontuberculous adenitis usually involves more than one gland and not infrequently both sides, and tenderness is the rule. The offending focus may be found in the tonsils or the teeth. Tuberculous

13. Heusinger: Halsfiemenfisteln des Menschen und Thiere, Deutsche Ztschr. f. Thiermed. 2:1, 1876.

adenitis is the most difficult to rule out. Of course, no effort should be spared on behalf of the patient to rule this out, for the stigma of tuberculosis in a young person is of considerable gravity. The fact that aspirated material may resemble tuberculous pus closely and be free from pyogenic organisms tends only to confirm the physician's original diagnosis of tuberculosis, unless he is aware of the possibility of its being a branchial cyst. The likelihood of the lesion's becoming infected and draining for an indefinite period also supports his delusion.

Though the atheromatous branchial cyst filled with grumous cheese-like material is glandular and firm and, if secondarily infected, is adherent to the surrounding structures and tender, yet in tuberculous adenitis it is more frequent to find other swollen glands or a group of matted glands. It is of some diagnostic importance that branchial cysts seem more common in the white race and tuberculous adenitis more common in the colored race. A cyst associated with an external fistula might be deceiving, but, as mentioned, a careful examination of the orifice of the fistula can be enlightening.

Cystic Hygroma.—Translucency is the most important differential feature and can be said itself to be diagnostic.

Thyroglossal Duct Cyst.—Such cuts are practically always in the midline and are so attached to the thyroid gland or trachea that they move forcibly during deglutition. Microscopically, it is frequently impossible to make the distinction.

Venous Hemangiomas.—These growths decrease in size on pressure, though one must be sure the contents of the tumor have not merely been squeezed into another compartment of the same.

Retropharyngeal Abscesses.—Such abscesses are painful and may exhibit swelling and tenderness on only a cursory examination of the pharynx.

Lipomas.—Lipomas, as well as other solid tumors, do not yield fluid material on aspiration.

For diagnosis, the demonstration of cholesterol crystals in the aspirated material of the cyst is helpful, though dermoid cysts produce this substance also.

Fistulas are sometimes injected with colored substances, such as methylene-blue (methylthionine chloride, U. S. P.), which, if the fistulas are complete, will issue from the internal orifice into the mouth. Bismuth paste has been injected and x-ray photographs obtained (cases 28 and 31). They have also been probed with small flexible filiforms, bristles of hair, etc. In one of our cases (fig. 9), we were able completely to pass an x-ray ureteral catheter and obtained roentgenograms, which were studied for the direction and curvature and relation of the tract to the hyoid bone.

PATHIOLOGY

In removing a branchial cyst, one often finds it attached at one pole to a fistulous tract, which most usually extends toward the tonsillar fossa. This tract often diminishes down to such fine caliber that it cannot be completely dissected. The wall of the cyst is usually smooth, though it may vary in thickness from that of tissue paper to 0.25 cm. It has been mentioned that one of these had the feel of lung, which was accounted for probably by numerous interlacing, tough, fibrous strands seen on the inner aspect of the wall, which were at first suspected of being hair.

Grossly, the content of the cyst is usually a thick, transparent, mucoid, sticky substance in those lined by columnar epithelium, while it



Fig. 9.—An x-ray picture of a patient with a ureteral catheter in a fistula. The markers designate the external orifice and the internal orifice in the tonsillar fossa.

is opaque, watery and milky or cheeselike and of all the consistencies between the two in those lined by squamous epithelium. The fluid content often can pass through a hypodermic needle, and though it may bear a striking resemblance to tuberculous pus, if some of it is placed in water, the shimmering lipid substance will be evident floating on the surface.

The cellular content has been found (Coplin²) to be as follows: (1) large cells resembling squamous epithelial cells, 93.7 per cent; (2) polymorphonuclear leukocytes, 1.8 per cent; (3) erythrocytes, 0.5 per cent, and (4) mononuclear leukocytes and unidentified cells, 4 per cent.

Gurlt, quoted by Senn,¹⁰ mentioned a great similarity between the contents of these cysts and the contents of ovarian cysts. He mentioned

the careful chemical examination made by Hoppe, which was as follows: 1.3953 Gm. of atheromatous material contained 0.2225 alcoholic extractive matter, 0.1235 ethereal extractive matter, 0.2005 aqueous extractive matter and 0.8555 insoluble matter. In these substances, he found leucine, tyrosine, cholesterol, myelin, palmitin and stearin.

Histologically, the walls of the cyst present many interesting features. The most usual observation is a well organized, stratified, squamous epithelium resting on a relatively thick band of lymphoid

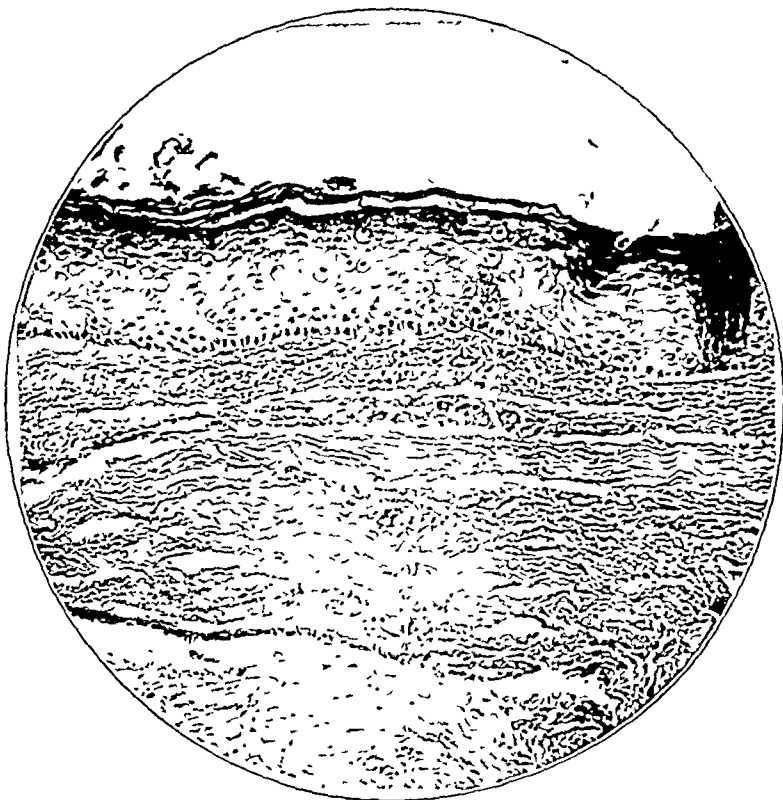


Fig 10—A photomicrograph of the wall of a branchial cyst to illustrate a stratified epithelium resting on a connective tissue base without the interposition of a band of lymphoid tissue. (Case 51, S. R.)

tissue, while beyond this is connective tissue, which may contain varying amounts of smooth and striated muscle (most likely extracapsular), and which is usually infiltrated to some extent with the elements of chronic inflammation—round cells, mononuclears and an occasional eosinophil leukocyte. The zone of lymphoid tissue may be entirely absent, the epithelium resting immediately on connective tissue (fig. 10). Again, it may be scant or abundant and with distinct and well formed lymph follicles (fig. 11). The epithelial layer, though in most cases

composed of stratified squamous cells, is now and then columnar with or without cilia (fig. 12).

One of our sections exhibited both the stratified and the columnar epithelium, while one showed well formed mucous glands just beneath the squamous epithelium. The differentiation from dermoids and other anomalies of earlier ontogenetic origin and their close simulation of the commoner epidermoids lacking hair, sweat glands,, etc., has been mentioned.

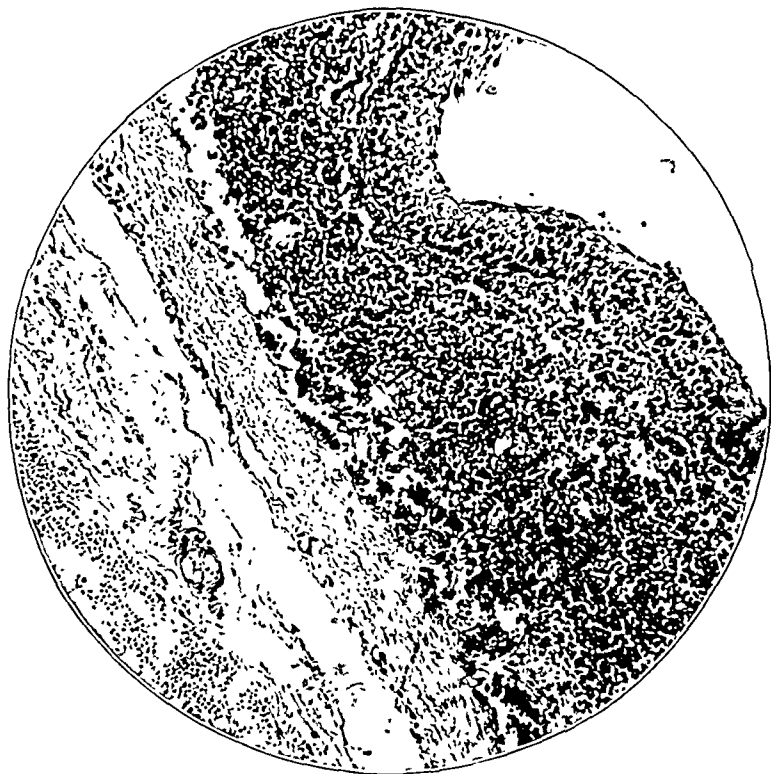


Fig. 11.—A photomicrograph of the wall of a branchial cyst to illustrate a stratified epithelium on a dense lymphoid tissue base. (Case 45, L. P.)

The stratified squamous epithelial layer appears like that of normal skin. There are, however, no papillae, except rudimentary ones, and the various layers are not discernible. The stratum germinativum or rete malpighii may be evident forming a row of cells with their oblong nuclei set perpendicular to the base, often containing considerable pigment and showing, as well as do many of their offspring, definite prickly cell characters. The nuclei are large, well defined and reticulated and contain one or more chromatin masses. They take the hematoxylin stain well and often maintain these characters well out to the stratum

corneum, where they suddenly cornify and are sloughed away. The cytoplasm stains darkly, appears finely granular and in places, owing to the prickled borders, is easily outlined. In some cases, the cells soon lose their original characteristics and become vacuolated long before reaching the stratum corneum. Though it has been mentioned (Coplin²) that the lymphatic layer is not especially vascular, we find the contrary to be true in our sections, many of them showing numerous vessels. It is true, however, that most of these also exhibit the elements of chronic inflammation.

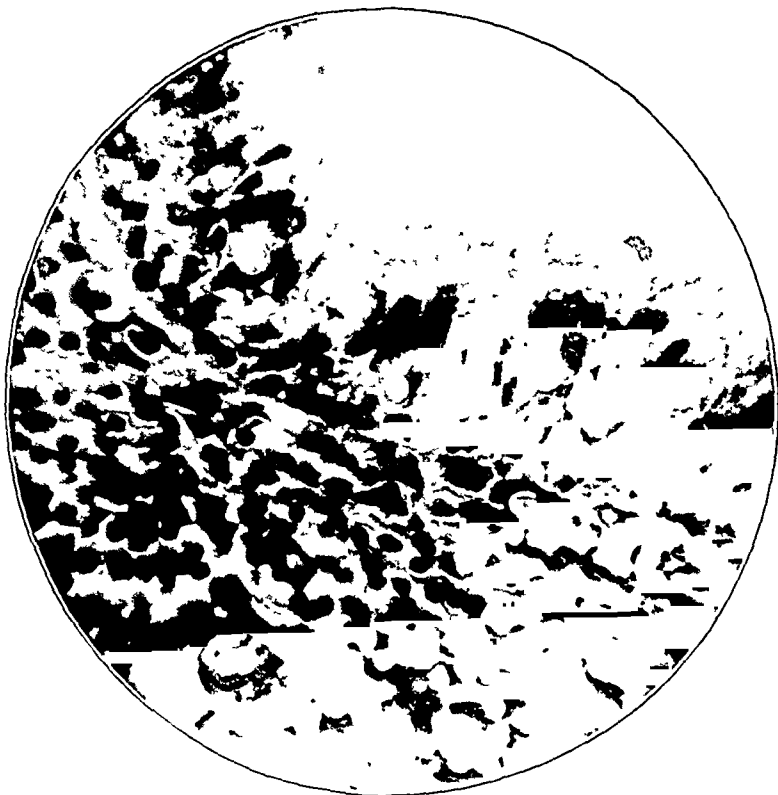


Fig. 12—A photomicrograph of the wall of a cyst to illustrate the ciliated columnar epithelium on a rather dense lymphoid tissue base. (Case 48, N. H.)

There are certain anatomic and histologic features of branchial cysts and fistulas that make their origin solely from branchial clefts more convincing than an origin from thymic stalk, as maintained by Wenglowski.¹⁴ The latter believed that cysts and fistulous tracts lined with stratified squamous epithelium are ectodermal and must undoubtedly be of cervical sinus (Halssinus) origin, while the anomalies

14. Wenglowski, R : Ueber die Halsfisteln und cysten, Arch. f. klin. Chir. 100:789, 1913.

and portions of the anomaly that are entodermal are of thymic stalk origin. He felt that the dense lymphoid tissue with sometimes definite lymphoid follicles and occasionally what appear to be Hassall bodies in the walls of cysts and fistulas is strong evidence of thymic origin. It



Fig. 13.—A photograph (natural size) of an atheromatous branchial cyst removed from the right submaxillary region of V. H. (fig. 14). The cyst has been ruptured exposing the grumous contents of desquamated epithelial cells and cholesterol crystals. The wall was lined with stratified squamous epithelium.



Fig. 14.—Patient V. H. with an atheromatous branchial cyst in the submaxillary region of the right side. A photograph of the gross specimen is shown in figure 13

seems, however, that, in view of the fact that cysts lined wholly by prickle cell stratified epithelium, and therefore of undoubted ectodermal origin, are commonly found exhibiting the dense band of lymphoid

tissue, the latter cannot be used to bear witness of thymic origin. For the thymic anlage cannot have had to do with such a cyst. Further, the cysts located as high as the region of the tip of the mastoid present the same histologic characteristics, and there is certainly no reasonable proximity of such a structure to the region of the assumed remains of the thymic stalk.

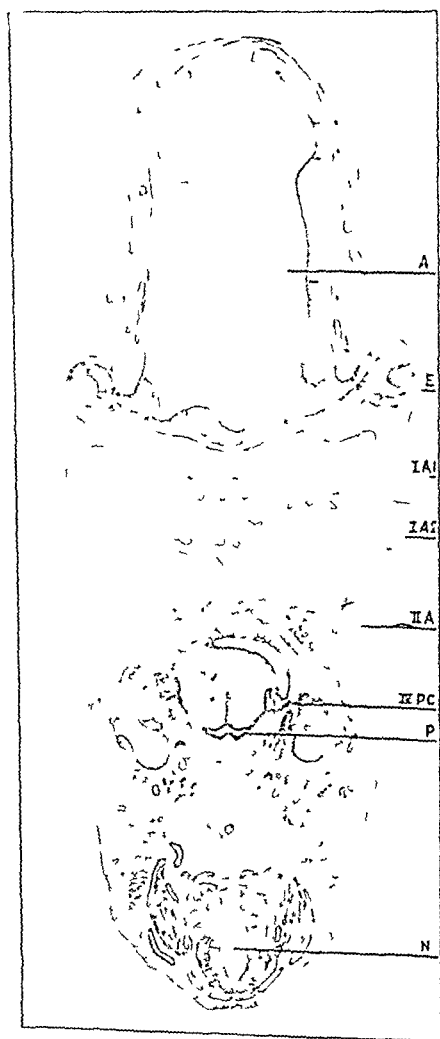


Figure 15

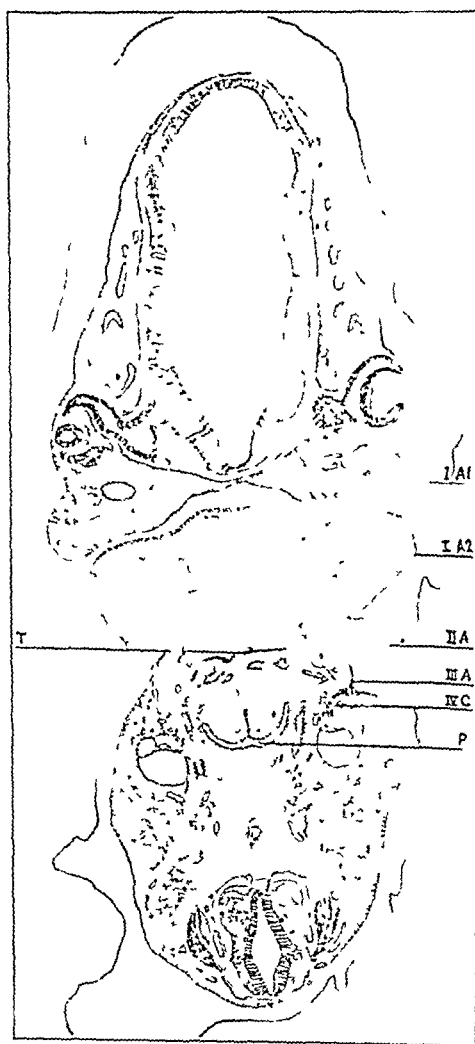


Figure 16

Fig. 15—*A* indicates the brain cavity, *E* the eye, *IA1* the superior division of the first branchial arch, *IA2* the inferior division of the first branchial arch, *IIA* the second branchial arch, *IVPC* the fourth pharyngeal cleft, *P* the pharyngeal canal and *N* the neural canal

Fig. 16—*IA1* indicates the superior division of the first branchial arch; *IA2*, the inferior division of the first branchial arch; *IIA*, the second arch; *T*, the thyroid anlage (the thyroglossal duct has disappeared at this state); *IIIA*, the third arch; *IVC*, the fourth cleft and *P*, the pharyngeal canal.

Wenglowski brought out that some of the external fistulas point downward instead of upward. One would expect this occasionally to be true, but so far as we were able to ascertain, no such fistula extended far enough to be convincing in this regard. In patient E. E. (case 58), the filiform, when passed into the left orifice, turned downward

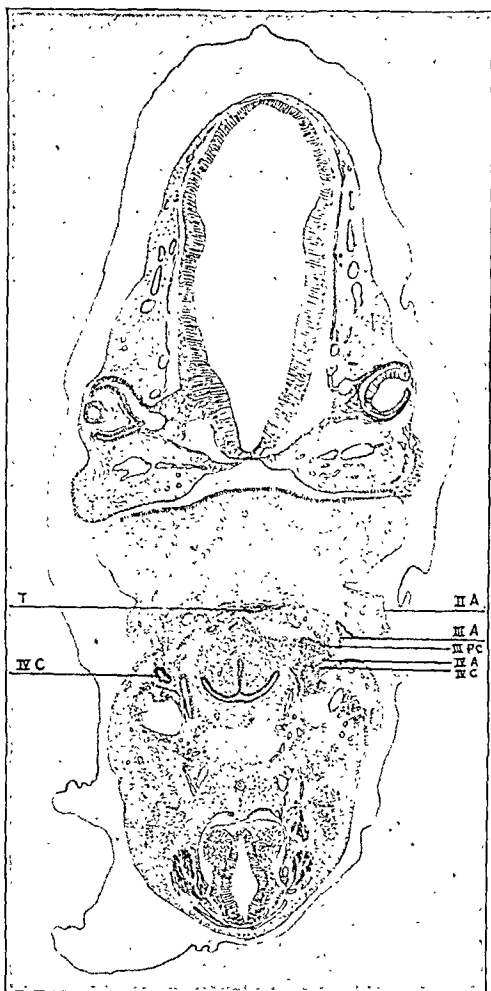


Figure 17

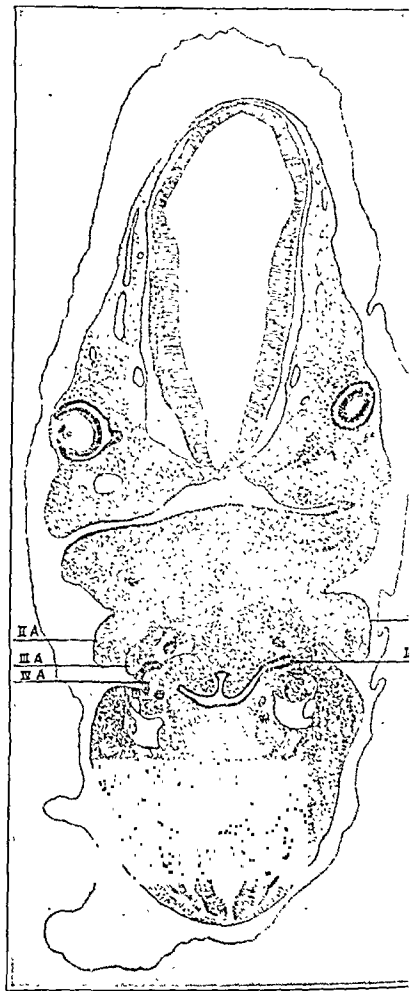


Figure 18

Fig. 17.—*IIA* indicates the second arch; *T*, the thyroid anlage; *IIIA*, the third arch; *IIIPC*, the third pharyngeal cleft; *IVA*, the fourth arch and *IVC*, the fourth cleft. The second arch is seen here to be growing downward to meet the body wall and inclosing the third and fourth arches forming what is known as the cervical sinus (Halssinus).

Fig. 18.—*IIA* indicates the second arch; *IIIPC*, the third pharyngeal cleft, now joining the pharyngeal canal; *IIIA*, the third arch and *IVA*, the fourth arch and cervical sinus shown on the right.

about one-half inch (1.27 cm.), but then turned up suddenly and joined a definite cyst. Also, if the remains of a thymic stalk played a rôle, cystic structures should occur anywhere from the final resting place of the thymus to the region of its origin. Langebeck, quoted by Senn,

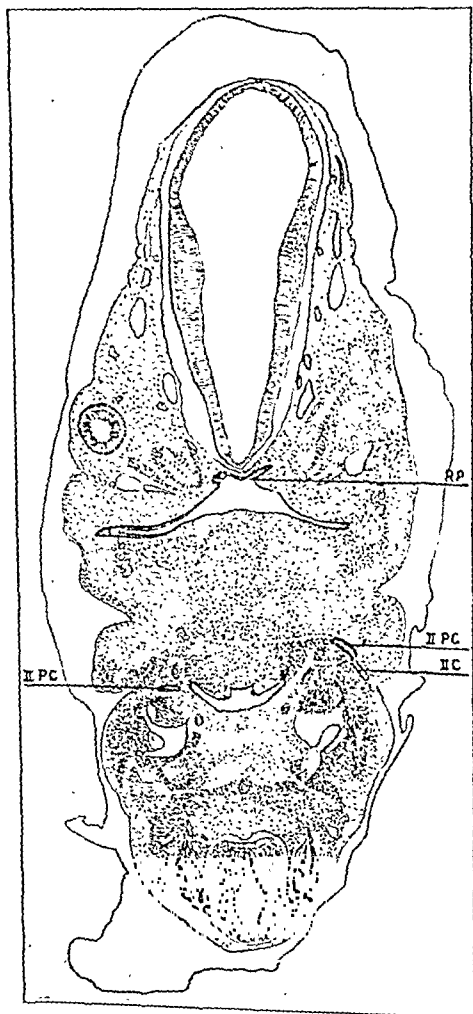


Figure 19

Fig. 19.—*RP* indicates Rathke's pouch; *IIPC*, the second pharyngeal cleft and *IIC*, the second cleft.

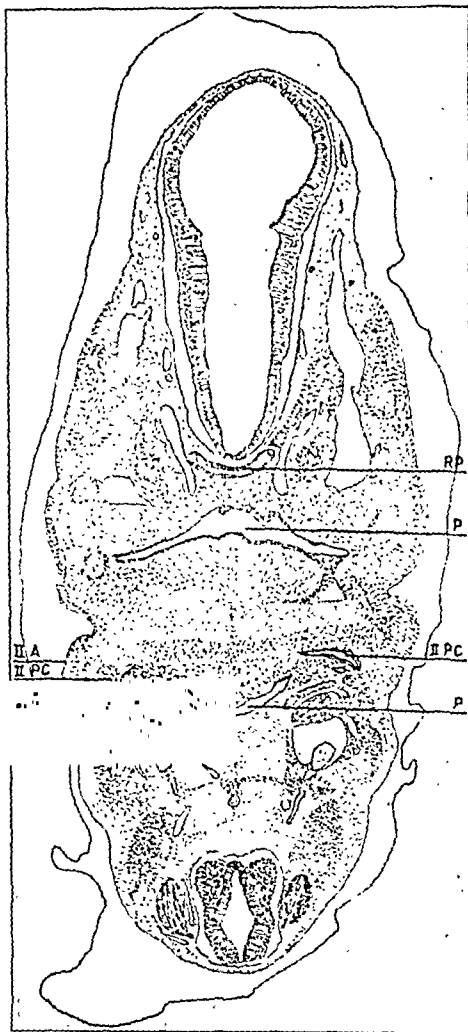


Figure 20

Fig. 20.—*RP* indicates Rathke's pouch; *P*, the pharyngeal canal; *IIPC*, the second pharyngeal cleft; *IIA*, the second arch and *IIC*, the second cleft.

stated that branchial cysts are frequently attached to the greater horn of the hyoid bone or to the thyrohyoid ligaments, localities that plainly indicate that they originated from remnants of former branchial clefts.

So far as fistulas are concerned, the third groove, being embryologic like the second, would seem to have the same chances of persisting, though so far as the external and complete fistulas are concerned, their tracts are practically always reported as coursing between the external and internal carotid arteries and having exit in the supratonsillar fossa and therefore must be of second groove origin. We are in poor position

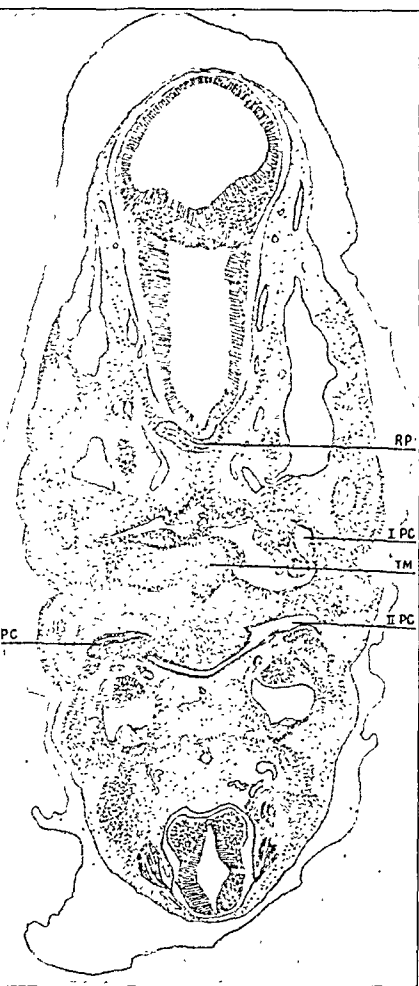


Figure 21

Fig. 21.—*RP* indicates Rathke's pouch; *IPC*, the first pharyngeal cleft on its way to meet the first outer cleft shown later, which forms the eustachean tube; *TM*, the tongue mass; *IIPC*, the second pharyngeal cleft.

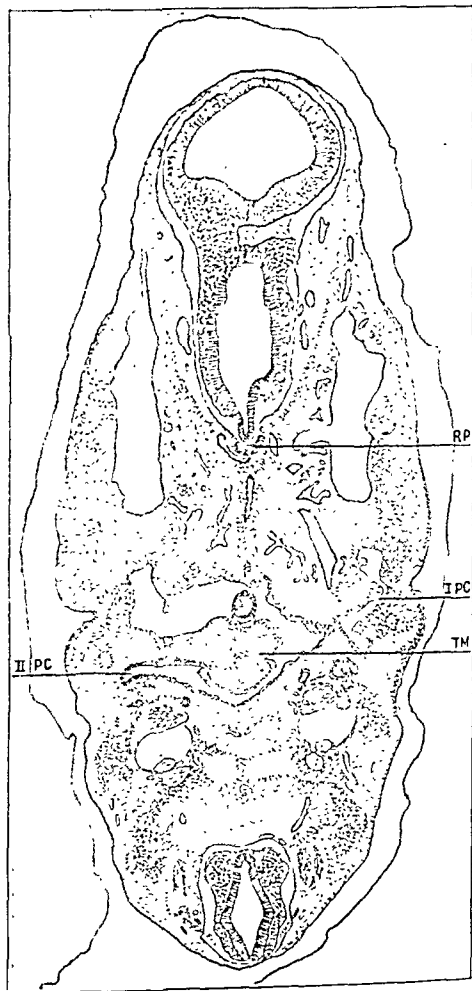


Figure 22

Fig. 22.—*RP* indicates Rathke's pouch; *IPC*, the first pharyngeal cleft; *TM*, the tongue mass and *IIPC*, the second pharyngeal cleft. The external first clefts are shown on both sides here, which will be met soon by the pharyngeal or internal first clefts. The first external clefts form the external auditory meatus.

to draw conclusions about incomplete internal fistulas. These must be far more common than one suspects, for it is not reasonable to suppose that they would ever be discovered if they remain relatively undisturbing to the patient. It is often extremely difficult to locate the internal orifices.



Figure 23

Fig. 23.—IPC indicates the first pharyngeal cleft and IC, the first (external) cleft. The membrane between IPC and IC forms the tympanic membrane.

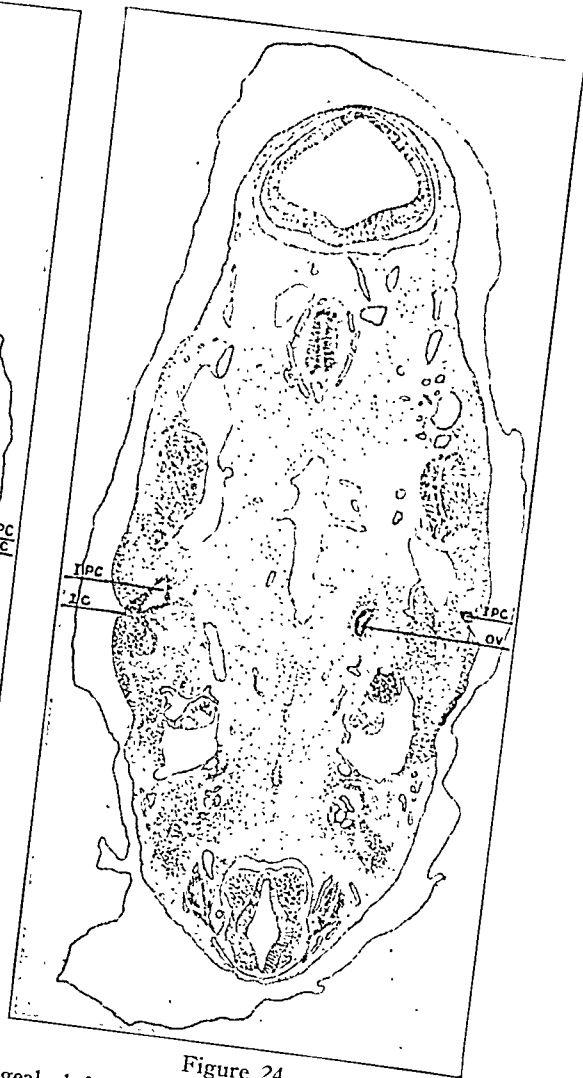


Figure 24

Fig. 24.—IPC indicates the first pharyngeal cleft; IC, the first (external) cleft and OV, the otic vesicle.

We have no report of a fistulous tract coursing inferior to the right subclavian artery or aortic arch, and believe, therefore, that the fourth groove is practically never responsible for such structures.

So far as the branchial grooves ever being normally patent is concerned, we find no indication of it in the serial sections of a 7.5 mm. human embryo (figs. 15 to 25). Owing to the manner in which serial sections are cut, one might get the impression of a patency from the pharynx to the outside but on following the true pharyngeal side

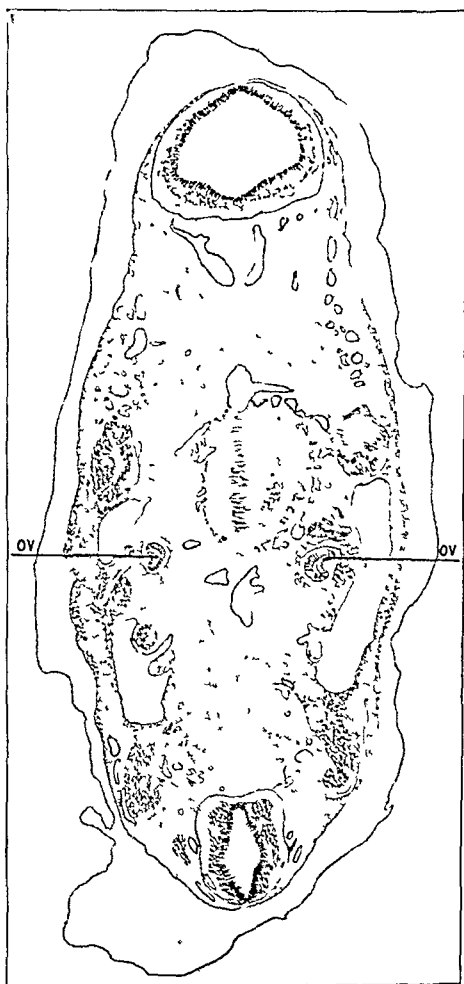


Fig 25—OV indicates the otic vesicle

of the groove this is seen not to be the case (i.e., the manner in which the fourth external cleft is cut on the left in figures 15 and 16 and on the right in figures 16 and 17 might be deceiving in this regard).

It seems far fetched to assume a tear of the groove membrane in early embryonic life as the cause of fistulas. In assuming this, one is practically limited to trauma, and it is hard to believe that in so small

an embryo, so well protected, trauma could be of just the extent to establish a fistulous communication between the pharynx and the outside. Even if such an accident occurred, there would be no logical reason for its persistence. Again, it cannot be supposed that cysts, the origin of which must be the same as that of fistulas, are established by tears of the groove membrane in a neck that has never presented the stigmas of external or internal fistulas.

There has been little contributed on the subject of the origin or existence of aural fistulas. The anomaly has usually been lightly passed over with the assumption that it originates in the first branchial groove.



Fig. 26.—Patient E. E. (case 58), with bilateral cervical fistulas and an aural fistula on the left. A urethral filiform is shown entering the external orifice and coming through the mouth having made its exit in the supratonsillar fossa.

It is difficult, however, to attribute it to such an origin when, as is known, the first groove normally persists in the formation of the external auditory meatus and the groove membrane in the formation of the tympanic membrane. It has been also suggested that fistulas, as well as cysts, in this region are the result of epithelial inclusions or of anomalous development of the several tubercles that go to form the pinna. The fistula was blind in all of our familial cases, was only an eighth to a quarter of an inch (from 0.3 cm. to 0.6 cm.) in depth and had never been the site of a discharge.

Histologically, these anomalies present none of the structures of advanced differentiation such as hair follicles or sudoriferous glands, though in one of our sections well formed mucous glands were contained in the cyst wall just beneath the lining epithelium. The explanation of this difference from teratomas and dermoids rests on the fact that the inclusions are made after the three germinal tissues have well differentiated. Branchial cysts are indeed, therefore, not greatly different from any of the commoner epidermoid cysts, i.e., the epidermoid cysts about the face and palms of the hands resulting from epithelial inclusions or bits of epithelium buried by trauma and subsequently continuing their active growth and desquamation. In the latter there is often, too, a marked lymphoid infiltration in the cyst wall, but so far as we know, no well defined lymphoid follicles.



Fig. 27.—Patient E. E., showing symmetry of the cervical fistulas.

TREATMENT

The treatment of branchial cleft cysts and fistulas may be dismissed with one consideration—complete excision of the epithelial wall. This may be simple for superficial cysts, but technically extremely difficult for deep cysts and fistulas. We feel that it is not advisable to inject the cyst with methylene blue at operation owing to the marked disadvantage of having the operative field stained with the dye should the cyst rupture. If the operator is anxious to determine a possible communication with an internally opening fistula, the disadvantage might be obviated by washing the dye out of the cyst, thereby leaving only its wall stained. The relation of branchial anomalies to the vital structures of the neck makes their dissection a tedious one, and it should be attempted only by those who are acquainted with the anatomic minutiae

of the neck; for, obviously, if the dissection is not complete, the technical difficulty of a second operation is increased many-fold.

Most of the commoner corrosive substances have frequently been injected into the cysts, but are invariably without effect.



Fig. 28.—Patient E. E., illustrating the external orifices of symmetrical bilateral cervical fistulas and an aural fistula on the left. The right cervical fistula was complete, while the left led to a cyst, which fluctuated from the size of a filbert to that of a hen's egg.

Figures 15 to 25 were selected from 200 camera lucida drawings prepared by Dr. H. J. Prentiss from serial sections made of a 7.5 mm. human embryo. The sections were 10 microns thick and the drawings



Fig 29—Patient C E, showing a cervical fistula and a probe in the aural fistula on the right.



Fig. 30—Patient W E, showing bilateral cervical fistulas and probes in bilateral aural fistulas.

made from alternate sections. This stage of embryonic life is about the optimum for the illustration of the branchial apparatus. The sections were cut in such a way that the two halves are not symmetrical. Also, it should be remembered that due to the marked flexion of the embryo ventrally, sections taken from ventrum to dorsum will progress caudalward in the head region and cephalicward in the tail region. The sections shown in figures 15 to 25 progress ventrodorsally.

REPORT OF CASES

The following group of cases, which occurred in a mother, two daughters and a son, present familial branchial cleft fistulas:

CASE 1.—E. E., a colored woman, aged 28, entered the hospital with a complaint of frequent sore throat for two or three years past, a lump in the left side of the neck of four years' duration and a discharging sinus on each side of the neck. The family history and the social history were essentially without bearing. She had



Fig. 31.—Patient B. E., showing a cervical fistula and a probe in the aural fistula on the right.

five children, living and well, and had had no miscarriages. She said that she had never had any signs or symptoms of venereal infection. She had noticed the sinuses in the neck from birth, and from time to time (about three or four times a year) had observed that they seemed to swell slightly just at the point of exit and that in a short time they broke down discharging a few drops of whitish, translucent material. She felt that the one on the right opened into the throat, for occasionally a foul tasting substance seemed to be ejected on the right side of the mouth. For the past four years, she had noticed a swelling in the left side of the neck, which varied from the size of a filbert to that of a hen's egg. The fluctuation in the size of this swelling had no relation to mastication. When the mass swelled to its maximal size, she experienced nervousness and palpitation of the heart. There seemed to be also some difficulty in talking; that is, her voice seemed hoarse. In addition to these symptoms, she experienced pain in the region of the left shoulder, which she herself attributed to the lump in the neck because it was present only when this lump was swollen to its maximal size.

Summary of Data in Sixty-One Cases of Branchial Cleft Cysts and Fistulas

Author	Age, Years	Sex	Fistula (Side of Neck Involved)	Cyst (Side of Neck Involved)	Duration	Location in Neck	Hereditary Tendency	Diagnosis	Operation	Result	Remarks	Pathology	
1. Crow, I. N.; J. Iowa M. Soc. 15: 521, 1923	48	W	M	Right	?	Tonsillar fossa	0	Correct	+	Well	Cleared white particles from throat at times; fistula from 2 to 3 cm. in length, emptying into tonsillar fossa	Stratified squamous epithelium; lymphoid near basement membrane
2. Whitacre, H. J.; Ann. Surg. 37: 86, 1903	5	W	F	Right	Since birth	Lower third	0	Correct	+	Well	Began after tonsillectomy....	Stratified squamous epithelium
3. Johnson ^c	24	..	F	Left	1.5 yr.	Middle third	0	Correct	+	Well	Discharging fistula at birth healed after six years; after four years more, became infected; between external and internal carotids	Pus was aspirated at one time, but at operation cyst contained 2 ounces of semigelatinous fluid; stratified squamous epithelium
4. Johnson ^c	14	..	M	Right	Since birth	Lower third	0	Correct	+	Well	Between external and internal carotids; no communication with pharynx	Pear shaped cyst; inner wall smooth and filled with mucus
5. Johnson ^c	17	..	F	Right	Since birth	Lower third	0	Correct	+	Well	Between external and internal carotids; no communication with pharynx	Cyst 5 by 1 cm., lined with stratified epithelium
6. Johnson ^c	21	..	M	Left	Since birth	Lower third	0	Correct	+	Well	Between external and internal carotids; no communication with pharynx; discharged seropurulent material for seven years; healed fourteen years, then broke down	Tract 3 by 1 cm., containing mucoid material; lined by squamous epithelium on lymphoid tissue
7. Johnson ^c	7 mo.	..	M	Left	Since birth	Lower third	0	Correct	0	Well	Had remained closed for one year when last heard from	
8. Carp ^a	5	..	M	Right	Since birth	Lower third	0	Correct	+	Well	Healed from time to time; first discharged at 2 years; paroxysms of coughing ceased after operation; between carotid artery and veins	
9. Jefferson ³	18	..	F	Right	6 wk.	Middle third	0	Correct	+	Well	Supposed to have followed trauma	
10. Jefferson ³	47	..	F	Left	5 yr.	Middle third	0	Correct	+	?	Tender and brawny; pus drained and later cyst excised; between external and internal carotids and connected to pharyngeal wall by stalk	
11. Coplin ²	36	..	F	Right	3 yr.	Upper third	0	Lipoma?	+	Well		Sac 7 cm. in long diameter; squamous epithelium on lymphoid base; contained many one, two and three nucleated epithelial cells and a few polymorphonuclears

No.	Patient	Age	Sex	Side	Duration	Location	Treatment	Result
12.	Bryan, A. D.; S. Clinic, Chicago 4-11, 1920	19	M	Left	2 yr.	Upper third	Correct +	Well
13.	Bailey "....."	17	M	Lower third	2 yr.	Tuberculous + adenitis	? Aspirated seven times; then cyst size of tangerine shelled out
14.	Bailey "	20	F	Left	12 yr.	Tuberculous + adenitis	? Aspirated five times; later, cyst size of egg shelled out
15.	Bailey "	27	F	Lower third	2 yr.	Tuberculous + adenitis	? Aspirated fifteen times; later, cyst size of orange shelled out
16.	Bailey "	35	M	Lower third	18 mo.	Tuberculous + adenitis	? Incised and drained; later, large cyst dissected out
17.	Bailey "	20	F	Lower third	14 mo.	Tuberculous + adenitis	? Aspirated five times; pus sterile; given tuberculin; later, egg-size cyst excised
18.	Bailey "	26	M	Left	14 mo.	Middle third	Tuberculous + adenitis	? Aspirated four times; later, orange-size cyst dissected out
19.	Bailey "	20	F	Right	10 yr. 4 mo.	Middle third	Correct +	? Cyst size of orange
20.	Bailey "	18	M	Left	Middle third	Correct +	? Cyst size of orange
21.	Bailey "	34	F	Right	Life	Middle third	Correct +	? Cyst size of orange
22.	Bailey "	40	M	Right	1 yr.	Middle third	Correct +	? Size of egg
23.	Bailey "	19	M	Left	3 yr.	Upper third	Correct +	? Size of tangerine orange
24.	Bailey "	21	M	Right	1 yr.	Middle third	Correct +	? Size of orange
25.	Bailey "	46	F	Right	2.3 yr.	Upper third	Parotid tumor	Hazelnut size
26.	Becker, J.: Beltr. Z. klin. Chir. 134: 170, 1925	24	M	Right	Life	Lower third	Correct 0	Methylene blue came out by tonsil
27.	Glover "	37	M	Left	9 yr.	Middle third	? +	? Patient thought tumor initiated when he was injured in oil field
28.	Meyer, H. W.: Ann. I. Surg. 11: 121, 1923	27	M	Left	Life	Lower third	Correct +	Bismuth paste injected; X-ray picture revealed complete fistula, with exit in tonsillar fossa; foul-smelling fluid could be expressed; the tract passed above the greater corn of hyoid bone
29.	Thomson "	35	M	Left	3 yr.	Middle third	Tuberculous + adenitis	Well Perforde swelling causing pain in the shoulder, husky voice, later dysphagia, dyspnea and aphonia; did not go between external and internal carotids, but into pharynx

Summary of Data in Sixty-One Cases of Branchial Cleft Cysts and Fistulas—Continued

Author	Age, Years	Race	Sex	Fistula (Side of Neck involved)	Cyst (Side of Neck involved)	Duration	Location in Neck	Inherited tendency	Diagnosis	Operation	Result	Remarks	Pathology
30. Seel	16	..	F	Left	16 mo.	Middle third	0	Tuberculous adenitis	+	?	Extended to bifurcation of carotid; patient was debilitated and had lost much weight	Stratified squamous epithelium
31. Eddowes	30	W	F	Right	Birth	Lower third	Grandmother	Correct	+	Good	Injected with bismuth paste; discharged white to yellow material; extended from lower two-thirds of neck to lateral wall of pharynx; incomplete	
32. Gilman	13	W	F	Right	Birth	Lower third	0	Correct	+	Good	Iodine and silver nitrate had been injected without avail; after being dissected, left jugular vein completely stripped and the styloid process, submaxillary gland and right wall of pharynx became visible in the wound; the cyst was adherent to the carotid sheath	Contained semisolid gruel-like material with cholesterol crystals
33. Langenbeck	17	W	F	Left	Since 12	Middle and lower thirds	0	Correct	+	Good	Adherent to carotid sheath, it had been only partially dissected out at first and then drained; later completely dissected out	
34. Langenbeck	20	W	F	Left	Since 9	Middle third	0	Correct	+	Good	Reached to cervical vertebra posteriorly	Contents revealed epithelial cells in a state of fatty degeneration
35. Schede	15	W	M	?	18 mo.	Middle third	0	Correct	+	Good	size of hen's egg; had been irritated by injections; indicates that injection of irritating substances is responsible for adherence	Contents revealed epithelial cells in a state of fatty degeneration
36. Schede	22	W	F	Left	Since 11	Upper third	0	Correct	-	f	Attached to sheath of carotid artery	Creamy, yellowish fluid, containing free fat and epithelia; walls studded with sebaceous follicles especially toward the carotid artery; portion attached to sheath of vessels contained plate of cartilage which resembled the cartilage of the ear; hence he called it "auricular teratoma"

37. Virehow.....	34	W	F	?	Since 14	Upper third	0	Correct	+	Good	When cyst was out, revealed esophagus, lateral wall of pharynx, carotid artery in hyoid bone; great horn of ruptured jugular vein was	Contents showed flat epithelial cells, cholesterol crystals, fat granules and a mass of debris, the products of epithelial degeneration; wall lined with stratified epithelium
38. Senn 10.....	36	W	F	Right	1 yr.	Upper third	0	-	Located over bifurcation of common carotid; pulsated distinctly and made a pressure against floor of mouth and larynx; size of hen's egg and protruded in floor of mouth and pushed tongue against palate	
39. Senn 10.....	22	W	F	Right	1 yr.	Upper third	0	Correct	+	Good	
40. Senn 10.....	25	W	F	?	4 yr.	Under chin	0	Correct	+	Good	
41. Wernher.....	Child	W	F	Left	Since birth	Lower, middle, upper thirds	0	Correct	?	
42. Smith, T. ^o	8 mo.	W	M	Right	Since birth	Behind ear	0	Drained	?	
43. Smith, T. ^o	3 wk.	W	F	Left	Since birth	Lower, middle, upper thirds	0	0	?	
44. Treves 11.....	Infant	?	F	?	?	?	0	0	?	
45. Hyndman, I. P.	18	W	F	Left	16 mo.	Upper third	0	Correct	+	Good	
46. P. B.	22	W	F	Left	11 yr.	Middle third	0	Correct	+	Good	
47. L. H.	24	W	F	Right	3 yr.	Middle third	0	Correct	+	Good	
48. N. H.	6	W	M	Left	5.5 yr.	Lower third	0	Correct	+	Good	

"Microscopic examination revealed it to be of branchial origin"

Dark-brown, reddish, syrupy fluid escaped through rupture

Stratified squamous epithelium; much lymphoid infiltration, with lymph follicles
Stratified epithelium; lymphoid infiltration

Stratified squamous epithelium
Stratified and columnar epithelium; chronically inflamed

Summary of Data in Sixty-One Cases of Branchial Cleft Cysts and Fistulas—Continued

Author	Age, Years	Race	Sex	Fistula (Side of Neck Involved)		Cyst (Side of Neck Involved)	Duration	Location in Neck	Hereditary tendency	Operation		Remarks	Pathology	
				Left					Correct	+			Result
49.	E. E.	32	W	F	Left	9 mo.	Upper third	0	Correct	+	Good	Size of hickory nut	Stratified squamous epithelium with well formed lymph follicles; contained cheesy material
50.	R. J.	32	W	F	Left	?	Middle, upper thirds	0	Correct	+	Good	Size of egg; at operation, it lay on the vascular sheath	Stratified epithelium with much lymphoid infiltration; contained mass of epithelial cells and cholesterol crystals
51.	S. R.	22	W	F	Right	2 yr.	Upper third	0	Correct	+	Good	Size of hazelnut; attached to small pedicle	Stratified epithelium and remnants of epithelial structures in wall
52.	M. W.	21	W	M	Right	3 mo.	Upper third	0	Correct	+	Good	About size of hen's egg; fluctuated in size; never painful	Cyst wall trabeculated with grayish fibrous strands; walls contained lymphoid follicles
53.	R. B.	19	W	F	Left	3 mo.	Upper third	0	Correct	+	Good	Contained a milky fluid; extended deeply to jugular foramen; never painful	Stratified squamous epithelium with lymphoid tissue and follicles in wall
54.	D. R.	18	W	M	Left	6 mo.	Upper third	0	Tuberculosis	+	Good	Reached to base of skull from angle of jaw and contained creamy fluid	Stratified squamous epithelium on a lymphoid tissue base
55.	K. E.	20	W	F	Left	2 mo.	Middle third	0	Tuberculosis	+	Good	Size of hazelnut; two firm glands attached; contained milky fluid	Stratified squamous epithelium on a lymphoid tissue base
56.	L. B.	14	W	F	Right	Right	10 yr.	Lower third	0	?	+	Size of golf ball; contained yellowish caseous material	Columnar epithelium on a base of fibrous tissue with a few lymphocytes
57.	L. G.	30	W	M	Right	2 yr.	Upper third	0	?	+	Good	Keloid developed in scar; would swell and discharge yellowish material; complete fistula discovered at operation	
58.	E. E.	28	C	..	Left and right	Middle third	See case reports					
59.	O. E.	3	O	M	Right	Middle third	See case reports					
60.	W. E.	5	C	M	Left and right	Middle third	See case reports					
61.	B. E.	6 wk.	O	..	Right	Middle third	See case reports					

The forty-six cases of branchial cleft fistulas reported in Virebow's Archiv fur pathologische anatomie und Physiologie for 1891 were not included in this table.

On examination, the external fistulas were seen, as shown in the photograph. Aside from a marked hypertrophy of the tonsils and some hypertension, the results of the physical examination were essentially negative. The tonsils were so large that the internal orifices of the fistulas could not be seen until after the probe was passed. A urethral filiform catheter was passed with little difficulty through the right fistula; it emerged in the supratonsillar fossa. The filiform entered the fistula on the left and pointed down about one-half inch (1.27 cm.), then turned abruptly up and entered apparently into a somewhat firm lump on the left side of the neck. The internal orifice was not found on this side. The filiform on the right was followed by an x-ray catheter, after the passage of which stereo x-ray pictures were obtained. After the catheter had been introduced one half to two thirds of the way in the fistula on the right side, uneasiness and coughing were induced. Feeling that the stiff catheter would distort the fistulous tract to some extent, we later decided to inject iodized poppy seed oil 40 per cent. But after two weeks the fistula had become obliterated to such an extent that it was impossible to inject the iodized oil. This patient also had a fistula, just anterior to the left ear, which was about one fourth of an inch deep (0.63 cm.). There was no discharge from the fistula. In fact, it had never been brought to the patient's attention.

CASE 2.—C. E., a colored boy, aged 3, had a fistula on the right side of the neck and a right aural fistula, as shown in figure 29. Otherwise he was normal. The cervical fistula, on pressure, emitted a drop of clear, mucoid, tenacious fluid. The discharge from this fistula to the time of writing had been slight.

CASE 3.—W. E., a colored boy, aged 4 years, 8 months, had bilateral cervical fistulas and bilateral aural fistulas, as shown in figure 30. The results of the physical examination were otherwise negative. One of the cervical fistulas, to the time of writing, had discharged several times without pain or swelling.

CASE 4.—B. E., a colored girl, aged 6 weeks, had cervical fistula and aural fistula on the right (fig. 31). She presented no other abnormalities. On pressure, a small amount of clear, mucoid fluid could be expressed.

The two remaining children did not present branchial anomalies.

CONCLUSIONS

1. Branchial cleft anomalies (cysts and fistulas) result from a failure of absorption of the included ectodermal and entodermal epithelium that is buried during the growth and fusion of the branchial arches in early embryonic life. This is most probably the sole explanation, the thymic stalk playing no rôle.

2. Branchial cysts, in truth, are epidermoid cysts of the neck whose parent epithelium was buried during the development of the branchial apparatus. Their characters are more varied, of course, than those of the commoner epidermoid or inclusion cysts owing to the activity of entodermal or ectodermal epithelium or both. Many of the submaxillary cysts and so-called ranulae are of branchial origin.

3. Branchial fistulas may be familial and hereditary, and they seem to be inherited through the mother only.

4. More attention should be given to the possibility that a tumor in the neck is of branchial origin, especially in view of their frequent simulation of tuberculous glands and their occurrence in early youth. This is enjoined even more by the fact that results from treatment are in proportion to the completeness with which the epithelial wall is excised.

5. An adequate and simple classification of the cysts would be (a) branchial cleft epidermoid cysts and (b) branchial cleft mucous cysts.

LYMPHATIC DRAINAGE FROM THE PERITONEAL CAVITY IN THE DOG *

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Accurate data concerning the extent and the routes of drainage from the abdominal cavity of patients with gastro-intestinal lesions are of extreme importance. Pulmonary involvement, so commonly associated with abdominal operations, is a sequela which may be explained by the lymphatic continuity of the two regions. Many experiments have been made in an effort to determine the site and rate of absorption from the peritoneal cavity and the routes through which such materials are removed. Cunningham¹ completely reviewed the literature which concerns these various phases of the problem.

In the hitherto published accounts of experimental studies on the method of lymphatic drainage following peritoneal absorption, more careful attention has been given to the cytologic problems than to the lymphatic paths which are involved; also to the manner in which the foreign particles within the peritoneal cavity get into the lymph stream, whether free and independent or in phagocytic cells, than to the distribution of the lymph channels throughout the diaphragm, mediastinum and pulmonary regions. In the process of absorption from the peritoneal cavity, the lymphatic tracts of the diaphragm are most extensively involved. From this muscular partition the lymph may flow either through the anterior mediastinum and its associated lymph nodes or, to a lesser degree, into the thoracic duct and thence to the venous circulation at the jugular subclavian confluence.

Our interest in the problem of peritoneal absorption grew out of a desire for more accurate knowledge concerning the lymphatic system of the diaphragm and its relation to the lymphatics of the lungs in the leading experimental animal, the dog. Excellent descriptions, adequately illustrated, of the lymphatic distribution in this region in man are available in standard textbooks on anatomy, but adequate descriptions of the system in this region in the dog are not available. Sisson² con-

* Submitted for publication, Oct. 4, 1928.

1. Cunningham, R. S.: The Physiology of the Serous Membranes, *Physiol. Rev.* 6:242, 1926.

2. Sisson, Septimus: The Anatomy of the Domestic Animals, ed. 2, Philadelphia, W. B. Saunders Company, 1914, p. 930.

tributed little if any data on the lymphatics of the diaphragm and their relations to the lung. Since the dog is being used more and more as an experimental animal, it is increasingly important to obtain such data. Furthermore, the exact relationship of the lymphatic system to the vascular system is inadequately understood. The fact that normal lymph so often contains large numbers of erythrocytes leads one to question the generally accepted statements that the lymphatic system is a closed one. Accordingly, it may be worth while to seek further detail bearing on this most important but little understood lymphatic organization.

Many excellent reports of experimental studies on the absorption of particulate matter from the peritoneal cavity, with special reference to the reactions of free phagocytic cells, are available. The mode of transfer of such particulate matter into the diaphragmatic lymphatics, whether through definite stomata as originally advanced by von Recklinghausen,³ or directly through the cell bodies, are among the questions discussed. MacCallum⁴ denied the existence of stomata and attributed absorption to the activity of free phagocytic cells. The pumping action of the respiratory movements facilitated the passage of these phagocytic cells into the lymph stream, although in the absence of such macrophages the mechanical factors involved literally forced free particles through the wall of the lymph channel.

Various injecting mediums have been used in the earlier studies of peritoneal absorption. Buxton and Torrey⁵ recovered nucleated blood cells from the mediastinal lymph nodes fifteen minutes after their intra-peritoneal injection into a guinea-pig. Bolton⁶ employed lampblack, bacteria and nucleated blood cells in his study of absorption, and concluded that the drainage is a purely mechanical process, the force being supplied by respiratory movements, and that the particles pass between the epithelial cells of the diaphragm. Bolton briefly commented on the position of the lymph channels which drain the diaphragm. Cunningham⁷ injected into the peritoneal cavity of cats a solution consisting of washed nucleated blood cells, unfiltered carbon particles and lamp-

3. Von Recklinghausen, F. T.: Zur Fettresorption, *Virchows Arch. f. path. Anat.* **26**:172, 1863.

4. MacCallum, W. G.: On the Relation of the Lymphatics to the Peritoneal Cavity in the Diaphragm and the Mechanism of Absorption of Granular Materials from the Peritoneum, *Anat. Anz. Centralbl.* **23**:157, 1903.

5. Buxton, B. H., and Torrey, J. C.: Absorption from the Peritoneal Cavity, *J. M. Research* **15**:5, 1906.

6. Bolton, Charles: Absorption from the Peritoneal Cavity, *J. Path. & Bact.* **24**:429, 1921.

7. Cunningham, R. S.: Studies in Absorption from Serous Cavities: IV. On the Passage of Blood Cells and Granules of Different Sizes Through the Walls of the Lymphatics of the Diaphragm, *Am. J. Phys.* **62**:248, 1922.

black granules in isotonic sodium chloride solution. In three minutes all three types of material had reached the anterior mediastinal lymph nodes, but were all free in the sinuses. The foreign particles had not been phagocytosed in their transfer to the lymph stream, but moved freely into the surface cells of the diaphragm. In Cunningham's study on the absorption from the peritoneal cavity in the fetus, respiratory movements seem intimately correlated with the extent of absorption. Such movements of the diaphragm literally force the particles into the cells where they are carried through the endothelium into the lymph duct.

Cunningham,¹ in a complete review of the physiology of serous membranes, concluded that at least a large proportion of the particulate matter passes through, and not between, the cells in the course of its absorption into the diaphragmatic lymphatics from the peritoneal cavity. He further concluded that one significant factor in the absorption of particulate matter through the mesothelial cells is by means of the pressure of the diaphragm on the intra-abdominal viscera. Florey,⁸ in studies on the rabbit, concluded that foreign particles pass from the peritoneal cavity between the mesothelial cells of the diaphragm into the lymphatic trunks and not directly through the cytoplasm of these cells. Florey supported the original thesis of MacCallum (1903), but did not substantiate the observations of Cunningham (1922). Poynter⁹ has conducted extensive experiments on the absorption of true solutions, colloids, bacteria and particulate matter from the peritoneal cavity, and concluded that lymphatic channels, except those related to the diaphragm, play but an insignificant part in the absorptive process. The venules of the omentum are shown by Poynter to be the more important avenue, because various colloidal particles have been recovered from the portal blood and the liver. The mesenteric lymphatics, the receptaculum chyli and the thoracic duct were never found to participate in the drainage from the peritoneal cavity. More recently Brown,¹⁰ in an experimental investigation to determine the value of lymphaticostomy, concluded that in rabbits the main path of absorption from the peritoneal cavity is by the thoracic duct, but in dogs and cats this route plays only a subsidiary part. He concluded that lymphaticostomy cannot be recommended in cases of acute peritonitis. Although we have observed the mode of absorption and the nature of the particulate matter in the lymph stream in a number of instances,

8. Florey, Howard: Reactions of, and Absorption by Lymphatics, with Special Reference to Those of Diaphragm, *Brit. J. Exper. Path.* **8**:479, 1927.

9. Poynter, C. W. M.: Peritoneal Absorption, *Proc. Staff Meetings, Mayo Clinic*, **2**:263, 1927.

10. Brown, K. P.: Peritoneal Lymphatic Absorption: An Experimental Investigation to Determine the Value of Lymphaticostomy, *Brit. J. Surg.* **15**:538, 1928.

we shall not report them here, since this paper is restricted entirely to a consideration of the lymphatic channels which are involved in the drainage of particulate matter from the peritoneal cavity in the dog.

METHODS OF STUDY

Various types of particulate matter have been used from time to time in the study of peritoneal absorption. Florey used hemoglobin, india ink, and suspensions of carmine and cream, but his best results were obtained by using finely particulate graphite, first described by Drinker and Churchill,¹¹ and known as "Hydrokollag 300." Higgins and Murphy¹² modified somewhat the method of making the suspension described by Drinker, and greatly reduced the interval required to perfect the final product. When made correctly and thoroughly centrifuged the final preparation is a homogenous mass of particles many times smaller than erythrocytes. The preparation may be injected directly into the blood stream of mammals without causing any reaction, and thus it provides an admirable means for the study of the reticulo-endothelial system. We have used the graphite preparation repeatedly for studies on the von Kupffer cells of the liver, the reticular cells of the spleen and the phagocytic cells of serous cavities, and have found it an entirely satisfactory injection mass.

OBSERVATIONS

If a given quantity of the final graphite preparation, the amount varying with the size of the animal, is introduced into the peritoneal cavity of a dog, the lymphatics of the diaphragm are soon visible with the injection particles. In periods ranging from ten minutes to an hour and a half the lymphatic channels on the pleural surface of the diaphragm are completely delineated (fig. 1). Muscular activity appeared to hasten the absorptive process for, in animals exercised during the interval following the intraperitoneal injection, the lymphatics were more readily and more completely filled. Massage of the wall of the abdomen and chest further facilitated absorption, and since the process seemed greatly retarded in animals suffering with distemper or other pulmonary disability, respiration played a significant part in the removal of such particulate matter from the peritoneal cavity.

One hour after the peritoneal injection of from 40 to 50 cc. of the graphite preparation, the lymphatic channels on the pleural surface of the diaphragm were well distended and their distribution could be

11. Drinker, C. K., and Churchill, E. D.: A Graphite Suspension for Intravital Injection of Capillaries, *Proc. Roy. Soc. London* **101**:462. 1927.

12. Higgins, G. M., and Murphy, G. T.: The v. Kupffer Cell in Common Laboratory Animals, *Anat. Rec.* **40**:15, 1928.

readily traced. Although some variation in the extent and distribution of the lymphatic pattern maintained in different animals, yet in the twenty-five dogs which comprised our series, the more characteristic picture is that shown in figure 1. It must be recalled that the lymphatics here illustrated are those functionally active in such normal absorptive processes, delineated only by the graphite and not by the injection method hitherto commonly employed.

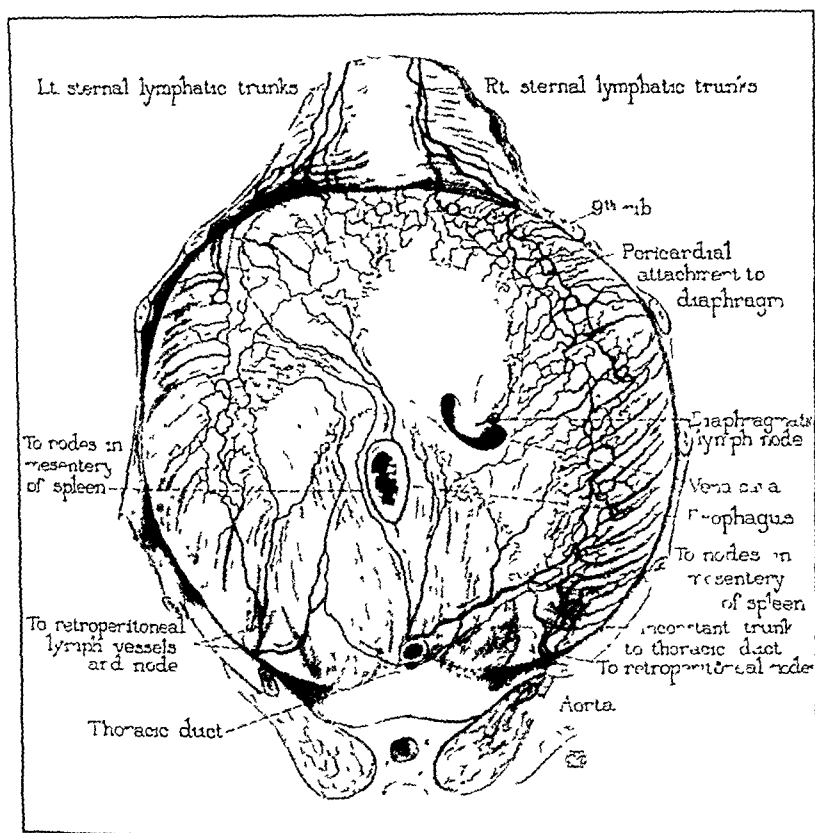


Fig 1.—The pleural surface of the diaphragm in a dog after the intraperitoneal injection of the graphite preparations. The lymphatic channels of the diaphragm are distended.

Figure 1 shows that the distribution of the lymphatic channels is much greater on the right hemidiaphragm than on the left. The reason for this is not clear, although the proximity of the large right hepatic lobe, providing greater contact surface during respiration, may be a factor. Prolonged massage of the left side of the chest and abdominal wall, however, failed to reveal more lymphatic channels on the left hemidiaphragm than could be seen during the normal process of absorption. The main collecting trunks of the diaphragm lie below the pleura,

on the muscle bundles, and pursue in general a diagonal course from the crura to the para sternalis. These larger channels, restricted for the most part to the medial portion of the muscular area, form a rather prominent plexus as they continue toward the sternum, and the smaller lymphatic vessels which arise along the costal attachment pursue more or less parallel courses and empty into the major plexus. The central tendon is relatively devoid of lymphatic channels. Smaller capillaries, however, are frequently discerned along the margins of the tendons, whence they empty into the larger vessels of the muscular portions and occasionally small channels drain across the central tendon from one muscular portion to another, particularly if the flow is toward the thoracic duct.

There are five drainage routes by means of which the absorbed material is removed from the diaphragm. The first of these is the sternal route, by far the more effective, which receives the drainage from the pars sternalis, pars costalis and to a certain extent from the pars lumbalis. From the standpoint of size and distribution the four remaining routes are apparently of equal significance in lymphatic drainage. The first of these, and perhaps physiologically and pathologically the most significant, comprise a variable group of small lymphatic capillaries which arise, partly in the pars sternalis, just ventral to the central tendon and partly from the muscular portion dorsal to the tendon. This group of small lymphatics, generally more conspicuous on the left side, leaves the diaphragm, courses forward along the pericardium, often parallel to the esophagus and the vagus, to the bronchial lymph nodes which lie dorsal to the base of the lung (fig. 2). Further drainage from this portion of the diaphragm is effected by a small lymphatic channel which usually arises in a small node and courses forward along the phrenic artery and nerve to a lymph node in the anterior mediastinum (fig. 2). The third route, effecting the anterior drainage of the lymph from the diaphragm is by way of the thoracic duct. The dorsal portion of the pars costalis and a portion of the pars lumbalis are drained by a varying number of small lymph channels which empty directly into the thoracic duct. The relative quantity of lymph which pours into the thoracic duct from the diaphragm is exceedingly small; in numerous experiments following the intrathoracic cannulation of the thoracic duct in animals which had received the peritoneal injections of graphite, free particles were rarely encountered in the thoracic lymph. In a single case, rapid appearance of the graphite in the thoracic duct suggested an unusual distribution of the diaphragmatic channels, and subsequent necropsy revealed an exceedingly large channel emptying directly into the thoracic duct. The thoracic duct is a variable structure in the different dogs. It is often double, somewhat

plexiform and passes forward usually to the right of the aorta and ventral to the azygos vein.

The other two lymphatic routes, draining a portion of the diaphragm, lead into the peritoneal cavity or into the retroperitoneal spaces dorsal to the two diaphragmatic crura. Of these two, the latter course is the more extensive and the more constant in its distribution. In figure 1 lymphatic channels are shown in the lower right and lower left margins of the diaphragm, which carry a portion of the lymph backward, dorsal to the peritoneum, to a large lymph node which lies in the retroperitoneal space just above the kidney; thence different channels pass obliquely to the cisterna. In figure 2 a group of three or four lymphatic channels are shown along the dorsal portion of the wall of the chest, coursing relatively parallel to the aorta. These channels, which readily distend with graphite when it is introduced into the peritoneal cavity, join those coming from the adjacent portion of the diaphragm and together course posteriorly to the retroperitoneal node described. Figure 1 shows also a group of three lymphatic channels which course over the dorsal half of the diaphragm and converge near the ventral margin of the aorta. These channels then course directly through the diaphragm, enter the peritoneal cavity, and may be traced directly to a lymph node in the mesentery of the spleen. Invariably these mesenteric nodes are black when the injection residue is washed from the peritoneum, but the extent of the vessels coursing from the diaphragm into the peritoneal cavity is a variable one. In certain dogs we were able to recognize them with great difficulty, and in others such peritoneal channels coursing directly from the diaphragm could be traced directly to the lymph nodes near the spleen, the kidney, and in some instances to the pancreas of Aselli.

We shall summarize briefly the lymphatic drainage from the diaphragm of dogs previously given injections of the graphite preparation. There are five routes through which such particulate matter is removed: the sternal, the pulmonary, the thoracic duct, the retroperitoneal and the direct peritoneal routes. Of these, the sternal route is essentially the most conspicuous and probably carries away four-fifths or more of the material removed from the peritoneal cavity. The pulmonary route is perhaps the next efficient, followed by the thoracic duct, the retroperitoneal lymph ducts, and, lastly, the direct peritoneal course, if one is to judge by relative distensibility following peritoneal absorption.

In the dog, then, the major drainage from the diaphragm is through the sternal lymphatics. In the slightly reflected portion of the sternum, as shown in the upper portion of figure 1, a group of three or four channels course from the diaphragm into the spaces between the intercostal muscles and continue forward, parallel to the sternal or thoracic

artery and vein. Occasionally, plexuses are formed by these channels around the blood vessels. These sternal lymphatic trunks continue into a series of two to four lymph nodes which lie in the interval between

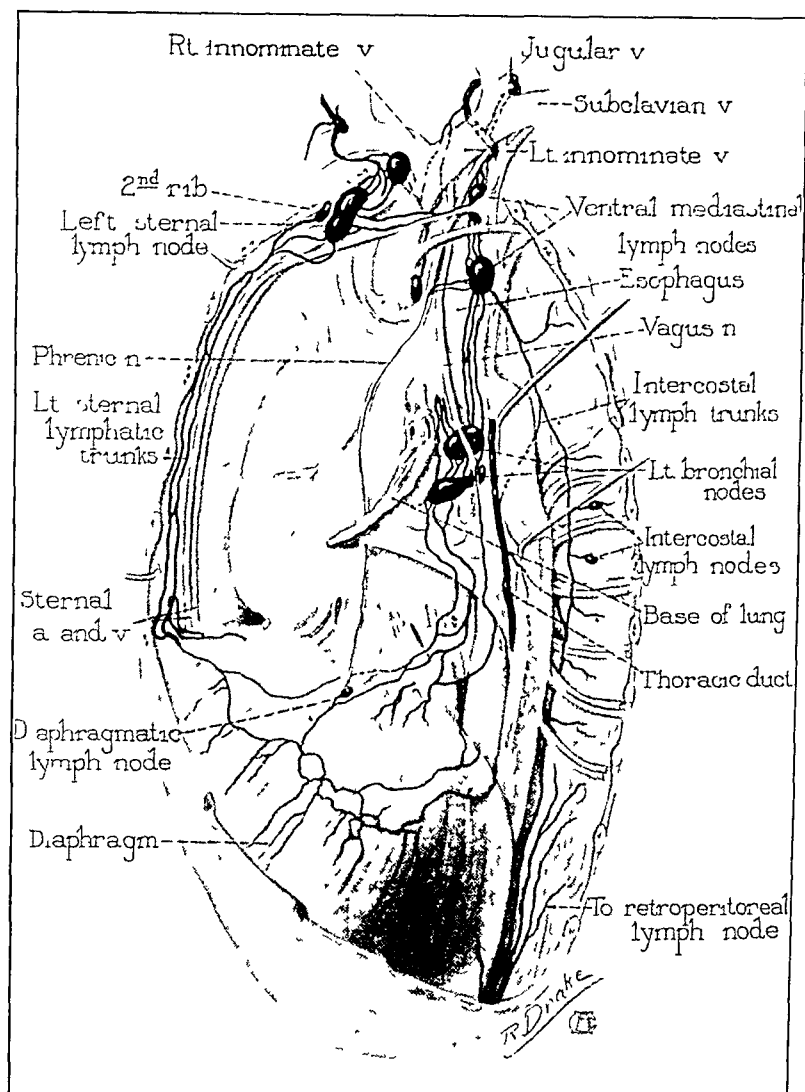


Fig. 2.—The right half of the thorax removed from a dog after intraperitoneal injection of the graphite. The lymph channels and nodes are shown, together with their relation to the thoracic duct.

the first and third ribs (fig. 2). Throughout their forward course the lymphatics on the two sides of the sternum are independent of each other, but in the region of these sternal lymph nodes numerous collecting

branches unite the two (fig. 3). Thence, the lymphatic drainage may be in any one of three directions: directly through collecting channels which course through the fascia along the right innominate vein to the right lymphatic duct and enter the venous system at the right jugular subclavian confluence; through anastomosing channels and additional nodes directly to the thoracic duct near its venous confluence, or by way

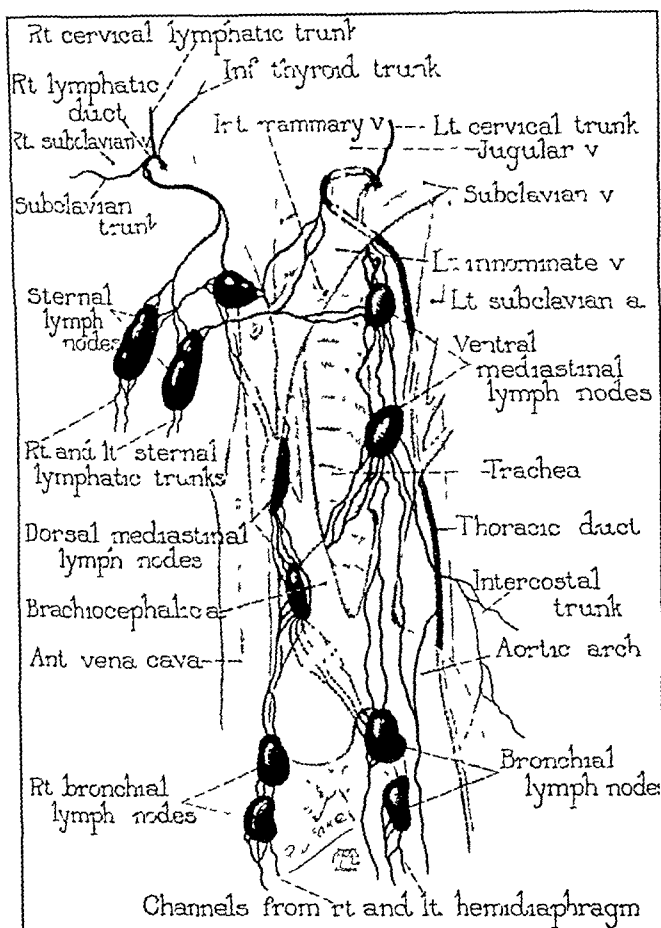


Fig. 3.—Dorsal view of the mediastinal region in a dog, showing lymph nodes and associated lymph channels in a dog given an intraperitoneal injection of the graphite preparation.

of a paratracheal mediastinal lymph node (fig. 3). The pattern of the lymphatic distribution in this region is a variable one, and an attempt will not be made to give in detail the various courses which our dissections have revealed. In general, the drainage from the right sternal lymphatics is to the right lymphatic duct; drainage from the left sternal lymphatics, with the exception of certain anastomoses, is toward the thoracic duct.

Figure 2 shows the drainage from the left side of the diaphragm through the pulmonary region. On the right side, the lymphatic channels from the diaphragm to the hilum of the lung are far less conspicuous, and yet in nearly every animal studied one or more such vessels were seen leading directly to parabronchial nodes on the right side. The lymph duct which courses forward over the pericardium, parallel to the phrenic nerve is invariably present. This empties directly into a paratracheal mediastinal lymph node, lying directly on the ventral surface of the trachea, somewhat anterior to the arch of the aorta. Other channels leave the diaphragm in the region of the central tendon, incline somewhat dorsally and course either through the pulmonary mesentery or along the esophagus parallel to the vagus nerve. This group of lymphatics enters the parabronchial nodes, usually two or three in number, which lie within the arch of the aorta just dorsal to the base of the left lung (fig. 2). We have never observed any direct lymphatic continuity between these diaphragmatic channels and the tissue of the lung. The pulmonary lymph channels, however, communicate directly with these parabronchial nodes and accordingly any retrograde flow of lymph would permit dispersion of the particulate matter of the peritoneal cavity within the lung. The discoloration of the lung in a number of dogs would suggest such a reversal, and yet the varying degrees of anthracosis which occur in the average dog render such a conclusion untenable.

Anterior to the parabronchial nodes, the lymph drainage continues by way of channels which pursue rather different courses in different animals. The more usual pattern encountered is that illustrated in figure 3. A group of from five to eight channels continues forward from these bronchial lymph nodes to a series of mediastinal nodes which lie in the fascia along each side of the trachea, the brachiocephalic artery and the anterior vena cava. A considerable portion of the lymph from the nodes on the left bronchus passes through channels which lie dorsal to the aortic arch, to the more posterior mediastinal node, which lies adjacent to the brachiocephalic artery, and receives the drainage from the right bronchial nodes as well. Other channels from the left bronchial nodes course directly forward ventral to the aortic arch and empty into the paratracheal node at a considerable distance anteriorly. Figure 3 shows that the drainage from the right side of the pulmonary region, and no doubt to a considerable extent from the left, empties into the venous circulation through the right lymphatic duct. The principal drainage from the left side, however, although exhibiting certain anastomotic arrangements with that of the right, is more largely forward through a series of two or three nodes which lie along the left side of the trachea and which ultimately connect by additional channels with the thoracic duct near its venous confluence.

The third anterior drainage route from the diaphragm is by way of the thoracic duct. As shown in figures 1 and 2, only a few small lymphatic channels ordinarily pass from the diaphragm into the thoracic duct. Accordingly, this route is of relatively small significance in the drainage of particulate matter from the peritoneal cavity. The duct, somewhat plexiform in arrangement, courses forward to the right of the aorta and ventral to the azygos vein, much as is shown in standard comparative textbooks, forms the characteristic ring around the base of the jugular vein and empties into the vascular circulation either at the subclavian confluence or into the left innominate or left brachiocephalic vein.

SUMMARY AND CONCLUSIONS

From this rather cursory survey of the anatomic relations of the lymphatic channels which function in the removal of particulate matter from the peritoneal cavity of the dog, it is evident that the thoracic duct plays a relatively insignificant part. Particulate graphite, when injected directly into the peritoneal cavity, is readily visible in the diaphragmatic lymphatics and the sternal trunks within from ten to twelve minutes in normal healthy dogs. In animals, however, in which the respiratory mechanism is disturbed, so that the normal excursion of the diaphragm is modified somewhat, the interval between the peritoneal injection and the appearance of the graphite in the sternal lymphatics is greatly prolonged. The injected graphite is visible in the sternal lymphatic trunks usually long before it can be identified in the cannulated thoracic duct. In only one dog of our series, a more or less rapid appearance of the pigment in the thoracic duct was explained at necropsy when an unusual distribution of the lymphatics of the dorsal portion of the diaphragm was discovered to include major channels which were directly confluent with the thoracic duct. Ordinarily, the lymph of the thoracic duct is colored only lightly and then only after prolonged intervals, when the lymphocytes within it contain large numbers of the graphite particles, probably phagocytes within the peritoneal cavity. With the animal under ether anesthesia, it is relatively simple to open the median line of the chest in the region of the first or second costal cartilages and thus expose the sternal or thoracic blood vessels. In this way the region may be watched and the first appearance of the black graphite in the clear lymph of the channel may be noted. Preparations made of the lymph coming through these channels show that the graphite contained within it is in the free particulate state, just as it was injected into the peritoneum. On the other hand, smears made from the lymph nodes in this region, as well as fixed paraffin sections, show that the material is both in the cells and in the free state, the particles having been phagocytosed by the large cells of the lymph node.

If in the same animal, or in one subjected to the same injection into the peritoneum, a cannula is introduced into the thoracic duct in the neck near its venous confluence, samples of lymph may be taken for analysis. Within thirty minutes, following the peritoneal injection, darkly colored lymph may be recovered from the thoracic duct in the neck. Analysis shows that the graphite contained therein is partly free and partly in the large lymphocytes. The cells containing the graphite are probably derived from the lymph nodes of the pulmonary, the tracheal or the sternal regions; the particles in the free state have passed directly into the lymph stream from the diaphragm.

By means of insufflation, one of us (Graham) was able to develop a technic whereby the thoracic portion of the thoracic duct could be cannulated and samples of lymph could easily be collected for analysis of cellular content. In a number of experiments, lymph was collected from the thoracic duct of dogs that had previously received a peritoneal injection of the graphite preparation. The sample taken immediately after the intraperitoneal injection was normal lymph with the usual number of small and large lymphocytes. During the first hour, long after the sternal lymphatics were black, there was no evidence of the graphite either in the free state or in phagocytic cells, yet there was an apparent increase in the number of large lymphocytes. An hour and a half following the injection, the larger cells of the lymph contained many granules of graphite, but the smaller cells were entirely devoid of them. There were no free particles in the lymph stream at this time. Subsequently, with an increase in the number of these large cells, small quantities of free graphite appeared in the lymph. Also, at intervals of about two hours following the injection, the larger cells contained the graphite in varying quantities, and in many cases the cytoplasmic bodies were literally packed with granules. Analysis of the peritoneal exudate showed masses of cells, similar to those recovered from the thoracic duct, packed with the graphite material. Unquestionably, these cells of the thoracic duct are identical with those in the peritoneal exudate, and they had probably entered the cisterna after phagocytosing the graphite in the peritoneal cavity. The particles of graphite which were encountered free in the lymph of the thoracic duct probably entered the duct through the few small channels coming from the dorsal margins of the diaphragm. Samples of blood taken from the femoral artery at this time contained occasional granules of free graphite, together with cells moderately packed with the injected material.

If one is to judge by the degree of physiologic activity and the number of lymph channels leading from the diaphragm it is apparent that the lymphatic paths coursing through the pulmonary region are more effective in removing foreign particles from the diaphragm than the thoracic duct. These channels are not large and by no means com-

parable to those which run along the sternum, and yet they are invariably present on the left side, coursing forward through the related mesenteries to the lymph nodes at the base of the lung, and usually are identified on the right side, although perhaps to a less degree.

In the removal of foreign particulate matter or bacteria from the peritoneal cavity, these pulmonary lymphatic routes are perhaps the most significant from the standpoint of pathology. Although these channels are not directly confluent with pulmonary lymph vessels yet they join with them in the nodes which lie at the base of the lung. In these nodes the lymph draining the two regions mingles and courses forward in the channels of the mediastinum. Accordingly, although direct pulmonary contacts with peritoneal drainage is not effected, nevertheless any disturbance in the flow or lymph coming from the lung, so as to involve stasis or even a retrograde flow, could well infect the lung with peritoneal organisms. These observations do not warrant such conclusions, for the pigmented lung so often encountered in these experimental animals has, of course, other explanations. The common pulmonary complications which accompany abdominal operations on dogs, however, may have their explanation in the lymphatic association of the two regions.

OLD NODULAR GOITER SURROUNDING TRACHEA, POSTERIOR TO THE CAROTID WITH THE ISTH- MUS POSTERIOR TO THE ESOPHAGUS

REPORT OF A CASE WITH SUDDEN DEATH FROM ACUTE ABSCESS*

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FORT WAYNE, IND.

History.—S., a man, aged 60, was brought to the hospital suffering from retention of urine due to an enlarged prostate. He had a large, nodular, hard goiter which was fixed and which he said never bothered him. However, on inquiry, it was found that for six or eight months he had been unable to breathe well when lying flat, and that for the same length of time his voice had been affected. There were no toxic symptoms. He had had the goiter "ever since he could remember."

Catheterization, with the usual treatment after ten days or two weeks, put the patient in a condition for operation. A two-stage prostatectomy was done on December 24 and January 15, respectively. The patient was making an ideal recovery until January 21, when he had a chill accompanied by severe pain in the right side of the goiter and a temperature of 103.4 F. He also complained of difficulty in breathing. On the next morning when I saw him, he was sitting in bed reading the paper, and complained only of some soreness in the right side of the goiter. The temperature dropped to normal that night, and on the 23d he was feeling quite well, with a slight elevation of temperature and some soreness still present in the goiter. Early the next morning (the 24th), he complained of severe pain in the neck and difficult breathing. Within ten minutes he was dead.

The nurse in charge of the floor also reported that the goiter was greatly increased in size, and that the man was cyanotic and evidently died from asphyxia. Both drains were removed from the bladder on the 23d when the cystotomy wound seemed to be in a good condition, and the drainage was satisfactory.

Autopsy.—Autopsy was performed three hours and thirty minutes after death. The bladder, the area around the prostate and the cystotomy wound were clean and normal. The abdomen was normal, except for stones in the gallbladder. Extensive pleural adhesions (old) were found on the left, and there were some on the right, also. The left ventricle was slightly hypertrophic. The cardiac vessels and valves were normal. No thrombus or embolus could be found.

The large goiter was uncovered with difficulty on account of close old adhesions; during the process of uncovering it, an abscess on the right side was opened and discharged more than an ounce of sanious pus, which was found to be streptococcic. Sharp dissection was necessary in removing the gland, which was closely adherent throughout its entire surface.

The right lobe (the larger) was crossed vertically on the outer anterior aspect by a white, flat band, which proved to be the carotid artery (fig. 1). This was separated from the gland, and the latter was removed in its entirety. The right lobe crossed over the trachea and was intimately adherent to the front of the

* Submitted for publication, April 2, 1929.

left lobe, and the isthmus was behind the esophagus. Thus, the esophagus and trachea were completely encircled by the goiter (fig. 2).

Figure 1 is a drawing that I made from memory immediately after the removal of the gland. Neither the artery, the trachea nor the esophagus was removed with the goiter but, to make the interpretation clearer, the drawing was made as though they had been. The artery should appear more flattened than it does in the drawing.

Figure 2 is a schematic representation of a cross-section showing the relation of the artery, the trachea and the esophagus to the goiter, also the location of the isthmus. Microscopic examination of several sections showed no malignant disease but old and recent inflammatory reactions.

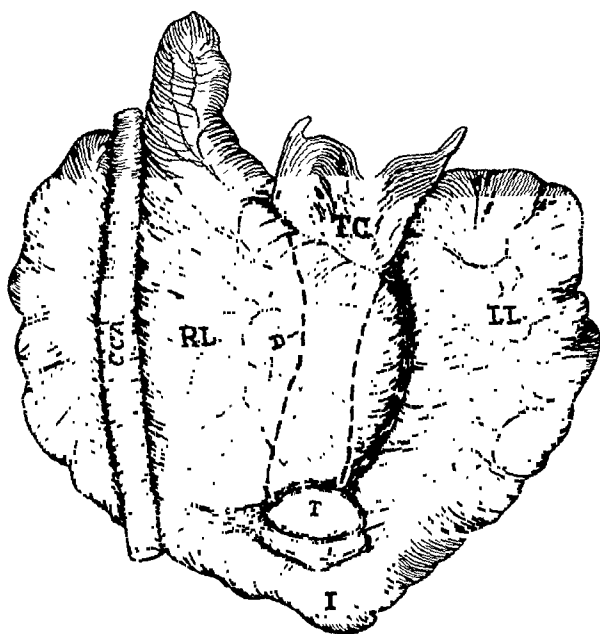


Fig. 1.—Drawn immediately after removal, from memory. *C.C.A.*, flattened carotid; *D.*, dent in trachea made by pressure of goiter; *T.C.*, thyroid cartilage; *T*, trachea; *E*, esophagus; *I*, isthmus; *R.L.* and *L.L.*, right and left lobes, respectively.

COMMENT

In my opinion, the sudden death in this case was due in the main to an acute streptococcic abscess. The source of the infection was not determined.

The universal close adhesions prove the existence of a long-standing, low-grade inflammation, an exacerbation of which may have been caused by the lowered resistance consequent on the urinary trouble, plus the operation. It should be added that examination of the specimen after removal showed several additional abscesses.

The asphyxia may have been in part, at least, due to pressure on the superior laryngeal nerve, as the abscess was located in the upper right aspect of the gland. However, the dent remaining in the trachea after the gland was removed shows that the capacity of that tube had been encroached on for a long time.

From the flattening of the carotid, one would suppose that the passage of blood through this vessel was considerably inhibited. If so, there were no clinical signs indicative of it.

I never saw the isthmus located behind the esophagus before, nor have I found a similar case reported, although, as is well known, unusual forms of this part of the thyroid are not infrequent. Absence of the isthmus or of one of the lobes is not extremely uncommon; it is quite possible that in the case reported, the isthmus and the left lobe were never developed and that what seemed to be the isthmus was really an extension of the right lobe of the gland, as was what I have named the left lobe.

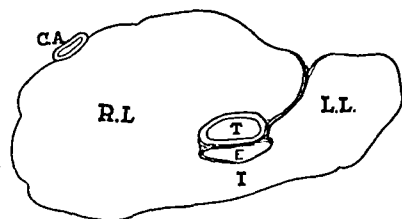


Fig. 2.—Schematic drawing of cross-section, showing relation of artery (C.A.), esophagus (E) and trachea (T) to the goiter. L.L., left lobe; R.L., right lobe; I, isthmus.

Pemberton¹ reported a case (fig. 3) in which there was a mass of thyroid tissue behind the trachea and esophagus which had developed from the right lobe and had formed a tumor on the left side from which the lobe had previously been removed. Hertzler sent me a photograph of a case much like Pemberton's (fig. 4), except that the growth was malignant.

Graham² referred to a case reported from Hoffman's Clinic by M. Willenbacher, in which the goiter completely encircled the trachea, producing dyspnea in a new-born child, and which was successfully removed forty-three hours after birth.

The distortion of the great vessels that was present in the case here reported has been seen in "several instances" in the Lahey Clinic³ in

1. Pemberton: Surg. Clin. N. Amer. 6:1278 (Oct.) 1926.

2. Graham: Practical Medicine Series, Surgery, Chicago Year Book, 1928, p. 211.

3. Clute, H. M., and Smith, L. W.: Cancer of the Thyroid Gland, Arch. Surg. 18:part 1, 14 (Jan.) 1929.

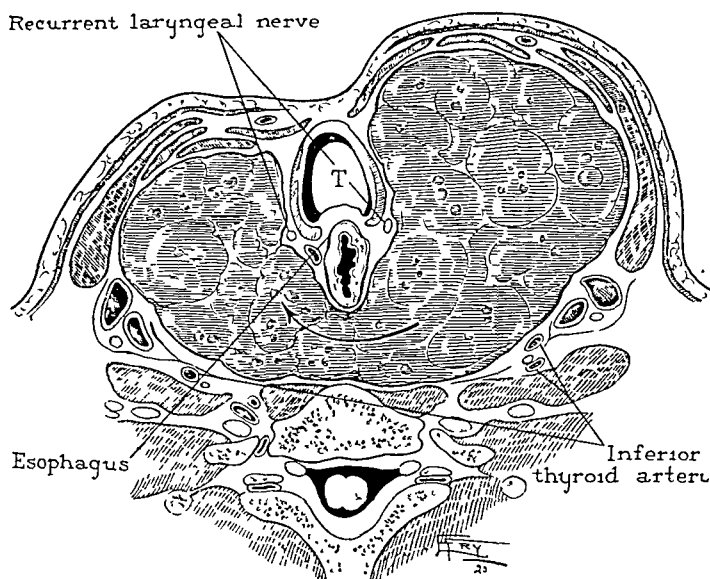


Fig. 3.—Cross-section of a huge retrotracheal projection, forming a tumor on the left side of the trachea from which the lobe had been previously removed. (From Pemberton: *Surg. Clin. N. Amer.* 6:1278 [Oct.] 1926.)



Fig. 4.—Postmortem specimen from Herten's case of sarcoma.

patients with cancer of the thyroid. Lahey⁴ said that they have never had a case like the one here reported. Albert Kocher⁵ referred to an outward displacement of the vessels so that the "carotid is felt in the external posterior portion of the tumor underneath the skin and along the outer border of the sternocleidomastoid muscle," but made no mention of such distortion as occurred in this case.

Crotti⁶ spoke of the displacement of the vessels much as Kocher did, but made no mention of anterior displacement.

Neither Ochsner⁷ nor Crile,⁸ in their works on goiter, mentioned derangement of the vascular relations such as is herewith reported.

C. H. Mayo⁹ said that he had seen "a few cases, not more than four" like the one reported here.

Crotti,¹⁰ said that he had seen eight or ten cases of "circular goiter in which the two lobes came in contact behind the esophagus."

SUMMARY

A case is reported of sudden death from asphyxia due to an acute streptococcic abscess engrafted on a chronic inflammation in an old, nodular, nonmalignant goiter, which completely surrounded the trachea and esophagus with the isthmus behind and the lateral lobes meeting in front of the trachea, and having the carotid vessels stretched over the front of the right lobe. It is probable that both the anterior dislocation of the vessels and the retrotracheal projection of the gland are more likely to occur in malignant goiters.

Cases similar in some respects are referred to, but after considerable inquiry by letter and research in the literature, no case like the one here reported has been found.

4. Lahey: Personal communication to the author.

5. Kocher, Albert, in Keene: *Surgery*, Philadelphia, W. B. Saunders Company, 1908, vol. 3, p. 359.

6. Crotti, Andre: *Thyroid and Thymus*, Philadelphia, Lea & Febiger, 1918, p. 124.

7. Ochsner and Thompson: *Thyroid and Parathyroid Glands*, St. Louis, C. V. Mosby Company, 1910.

8. Crile, G. W., and his associates: *The Thyroid Gland*, Philadelphia, W. B. Saunders & Co., 1922.

9. Mayo, C. H.: Personal communication to the author.

10. Crotti: Personal communication to the author.

THE EFFECT OF INTRABRONCHIAL INJECTIONS OF IODIZED POPPY SEED OIL 40 PER CENT

AN EXPERIMENTAL STUDY ON DOGS *

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CHICAGO

When iodized poppy seed oil 40 per cent was first advocated in intrabronchial instillation for the purpose of lung mapping, there seemed to us to be several theoretical objections. One of these was that a fibrosis of the lungs would be produced as a result of prolonged presence of an intrabronchial foreign body (iodized oil). Another was that bronchitis or bronchopneumonia would develop due to the transplantation of bacteria from the pharynx into the finer bronchioles by means of the oil. Long before we found experimentally that this second objection was theoretical only, we were convinced by reports of the clinics in which iodized oil 40 per cent had been taken up enthusiastically from the start that bronchitis and pneumonia did not follow its use.

The validity of the first objection, however, seemed to us to be strengthened as we began to see patients a year or two after the injection of iodized oil in whom traces of the oil remained visible roentgenographically. Also, Pinkerton¹ reported several cases of children in whose lungs marked fibrosis had occurred following the aspiration of small quantities of petrolatum which had been instilled into the nose for some local nasal condition. Finally, in our own hospital, Dr. Irving Stein found marked fibrosis of a fallopian tube which contained iodized oil several months after the oil had been instilled into the uterus for the purpose of mapping the uterine cavity and tubes.

EXPERIMENT

Our experiment consisted of intrabronchial injection of a small quantity of iodized poppy seed oil 40 per cent into dogs; the animals

* Submitted for publication, Jan. 15, 1929.

* From the Nelson Morris Institute for Medical Research of the Michael Reese Hospital, and from the Department of Experimental Surgery, University of Illinois.

1. Pinkerton, H.: Oils and Fats; Their Entrance Into and Fat in Lungs of Infants and Children, *Am. J. Dis. Child.* **33**:284 (Feb.) 1927.

were then killed at various intervals from a few days to seven months after the injection, and the lungs were studied roentgenographically, macroscopically and microscopically.

The technic carried out was identical in all dogs.

The animals were given hypodermic injections of morphine of sufficient strength to make them drowsy and docile, but not enough to put them to sleep.

They were placed on a fluoroscopic table and strapped to a board. Their mouths were held open by an assistant, and a tube (soft rubber French catheter no. 12)



Fig. 1.—Roentgenogram taken immediately after the injection of iodized oil into the lower branch of the right bronchus.

was quickly slipped through the posterior pharynx into the trachea and fed downward until its tip was in one or the other of the two main bronchi. Then from 5 to 20 cc. of iodized oil was injected into the bronchus under fluoroscopic control. The amount varied according to the size of the dog. Sufficient iodized oil was injected to outline clearly the bronchus and bronchioles of one or two lobes of a lung. The catheter was withdrawn and a roentgenogram immediately made.

The dogs were allowed the liberty of the kennels. At frequent intervals, roentgenograms were made.

The dogs were killed at lengths of time varying from a few days to seven months after the injection of iodized oil. A careful and complete autopsy was

done on each dog. The lungs were removed in toto, and roentgenograms were made before they were examined and sectioned.

Sections were made from every lobe of each lung and were stained with hematoxylin and eosin and sudan III (fat stain).

The control consisted of dogs killed for other experimental work. The lungs were removed in toto; roentgenograms were made, and the lungs were sectioned as in the experimental dogs.

RESULTS

Only two of the twelve dogs developed pneumonia—one dog a few days after injection and one several months after. We feel that these

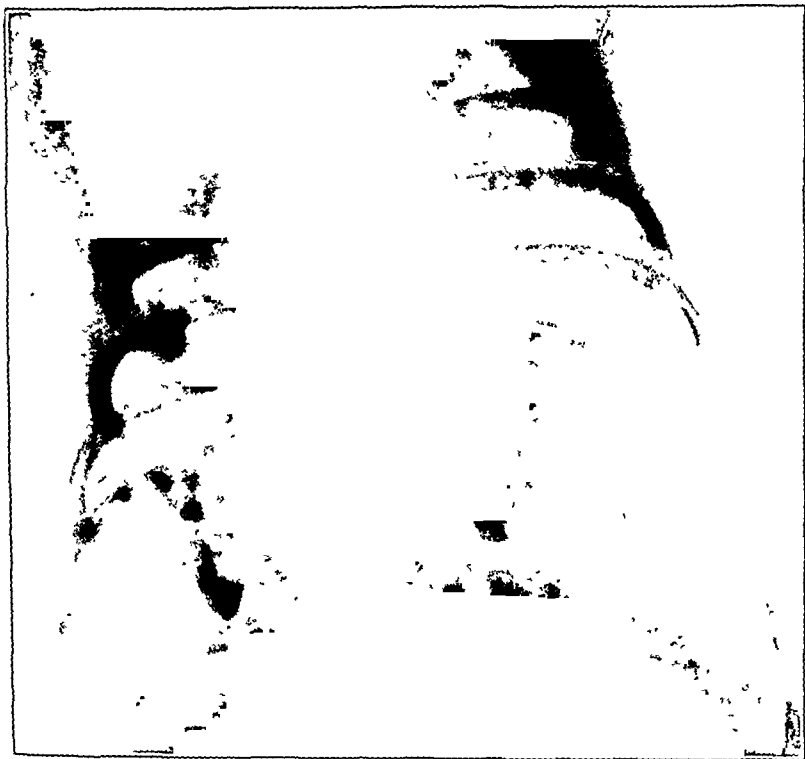


Fig. 2.—Picture of same dog in figure 1 taken four months later, showing retention of the iodized oil into the lower part of the right lung, and also the retention of the same material in the upper lobes.

two deaths have no bearing on the experiment, as in all our dogs the mortality from pneumonia during the winter of 1926-1927 was greater than this; furthermore, one of these dogs died in an epidemic which killed nearly all the dogs in the kennels at that time.

The fact that ten of twelve dogs did not develop pneumonia would have led us to discard the theoretical objection that iodized oil might cause pneumonia, if the clinical evidence had not already caused us

to do so. Macroscopically, only one dog showed signs of marked pulmonary fibrosis and scarring. This was in a dog in which the iodized oil had been injected one month previously. The appearance of the lung suggested a much older process, and the fact that we have seen dogs into which injections had never been made and which had similar lesions leads us to the conclusion that the fibrotic changes in this case cannot be traced to the iodized oil.



Fig 3—Roentgenogram of lung removed after the dog was killed six months after injection, showing retention of iodized oil

In almost every instance, the oil did not remain in the lobes injected but was quickly dispersed. In every instance almost all of the oil had disappeared by the time the second roentgenogram was taken.

In every case, small traces of iodized oil were seen roentgenographically in the lungs removed at autopsy. That includes the dog killed after almost seven months.

The results of the microscopic examinations were as follows:

The lungs of the dogs into the bronchial tree of which iodized oil had previously been injected did not differ grossly in any way from the

lungs of control animals. Microscopically, slight changes were present in the dogs given iodized oil. These changes were not constant in all the sections and did not vary in degree in any single section. Sections taken from those areas which showed a slight degree of mottling in the roentgenogram taken of the bare lungs after autopsy did not present signs or changes any more unusual than those in areas which were clear in the roentgenograms.

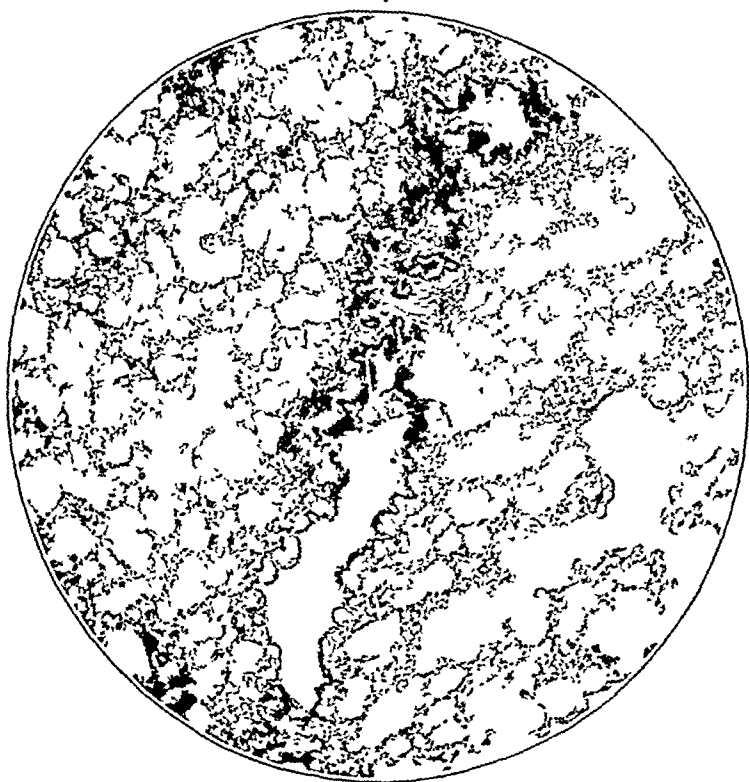


Fig. 4.—The portion of the lung which on roentgen examination was shown not to contain iodized oil. It is impossible to distinguish this section from sections of the control animals.

In sections stained with hematoxylin and eosin in both the dogs given iodized oil and in the control animals, a moderate number of large mononuclear phagocytes containing small particles of pigment occurred beneath the pleura. The number and distribution of these cells were about the same in the two sets of dogs. These cells often occurred in the region of small anthracotic areas, or occurred singly.

In the animals given iodized oil the terminal bronchioles were slightly more prominent than those of the controls, and there occurred a slight

increase in the thickness of the wall and a not prominent infolding of the epithelium. The number of lymphocytes in the walls of the bronchi was about the same in the two sets of animals.

In the dogs given iodized oil, small focal areas of fibrosis occurred occasionally beneath the pleura and about the terminal bronchi, and while similar areas occurred in the control animals, their frequency and size were slightly more prominent in the dogs given iodized oil.

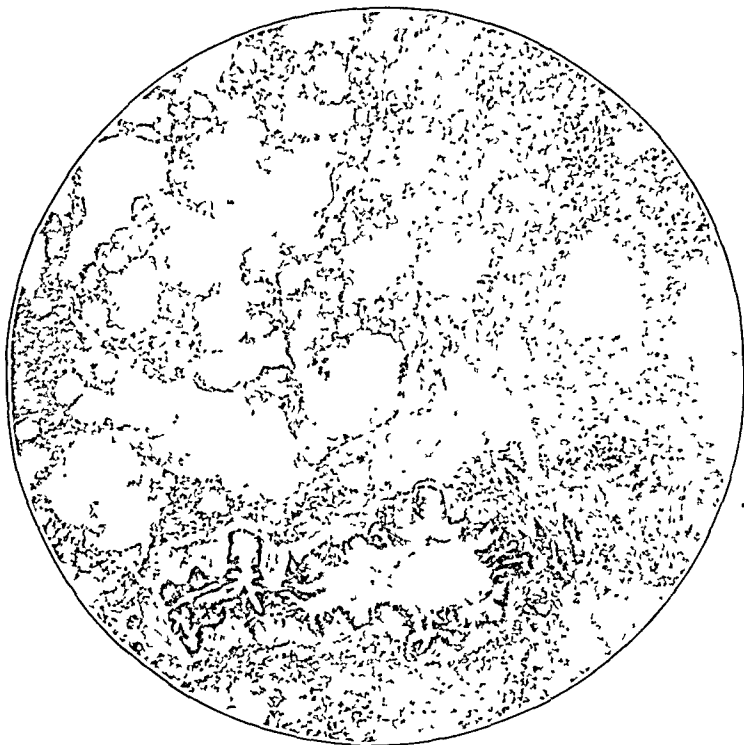


Fig. 5.—The lower lobe of the right lung, showing a slight thickening of the parenchyma. In the control dogs, apparently normal lungs showed areas indistinguishable from these.

In sections stained with sudan III, the number of macrophages containing small refractile globules of fat were slightly increased in the dogs given iodized oil. These macrophages occurred beneath the pleura, usually about a small area of anthracosis, but frequently appeared singly. An occasional lining alveolar cell containing small fat globules was present.

The larger bronchi of the dogs given iodized oil infrequently showed fat within the wall. This small amount of fat was located within the fat cells.

The conditions just described were not prominent in any of the sections taken from the lungs of dogs given iodized oil. They were present to a slightly less degree in the lungs of control animals.

Our results have led us to drop our theoretical objections to the use of iodized oil. Our results correspond with clinical experience and also with experimental observations published by others.

We were keenly interested in the result of Pinkerton's² experimental work. He showed results almost identical with our own when iodized oil was used, and results similar to those found in the lungs of children when mineral oils were used. He advanced the explanation that the difference in the reaction might be explained on the basis of the presence of specific ferments-lipases. At the suggestion of Dr. Schultz, the director of the Nelson Morris Institute, we attempted to show the presence of these ferments in lung tissue. However, the usual methods did not give results, showing that if these ferments do exist in lung tissue they exist in small quantities, perhaps in quantities not greater than those found in the circulating blood.

SUMMARY

Instillation of iodized poppy seed oil 40 per cent into the bronchial tree of dogs is not followed by pneumonia nor, as far as we could see, by any acute cellular reaction.

Most of the iodized oil is speedily expelled by coughing.

Small amounts of the oil are retained for at least seven months.

The presence of this iodized oil apparently does not cause a definite foreign body reaction.

2. Pinkerton, H.: Reaction to Oils and Fats in Lungs, Arch. Path. 5:380 (March) 1928.

INTESTINAL OBSTRUCTION

EXPERIMENTAL STUDIES ON TOXICITY, INTRA-INTESTINAL PRESSURE AND CHLORIDE THERAPY *

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In spite of the large amount of experimental and clinical work done on intestinal obstruction, there are still numerous insular concepts of the cause of death, and there are differences of opinion as to treatment. There have been several excellent reviews of the literature during the last few years, and Cooper has recently published an admirable analysis of the situation from the experimental evidence at hand. Since this literature is available, we shall not attempt to review past evidence but shall report the results of our experiments and our deductions as to the manner of treatment likely to be most beneficial for patients having intestinal obstruction.

There is general agreement that simple obstruction differs materially from obstruction with strangulation. This study deals only with simple obstruction.

There have been three primary purposes in these experiments: (1) to determine the toxicity of the content of obstructed intestine when it is present in obstructed and nonobstructed bowel; (2) to determine the effects of varying intra-intestinal pressure on the length of life after obstruction is induced, and (3) to determine the therapeutic value of sodium chloride under varying conditions of intra-intestinal pressure.

The attempt to answer these questions has necessitated inquiry into several subsidiary issues which will be discussed as they appear.

Rabbits have been used as the experimental animals. They are not so satisfactory to use as dogs, for they are more delicate and live a shorter period after obstruction. This disadvantage is more than offset in these particular experiments by the fact that rabbits do not vomit and therefore their intra-intestinal pressure can be controlled.

TECHNIC OF PROCEDURES

All operations, except the second stage of some jejunostomies, were done with the animals under ethylene anesthesia with no preliminary medication. The animals were denied food for forty-eight hours but were allowed water preoperatively. Operations were performed under aseptic precautions, and virtually no wound infections developed.

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* From the Laboratories of Columbia Hospital.

Obstructions were created in two ways. Temporary obstruction was produced by making an aperture in the mesentery just beneath the bowel and passing a one-fourth inch rubber band through the opening. The ends of the rubber band were brought out through stab wounds in the ventral abdominal wall about three eighths of an inch apart. The ends of the band were then sewed together applying sufficient tension to compress the intestine so as to occlude the lumen but not enough to destroy the blood supply. This tension was applied with the intestine under observation. When the obstruction was to be released, the rubber band was cut and removed without anesthesia. Usually the intestinal contents could immediately be heard passing beyond the point of obstruction. Permanent obstruction was produced by tying umbilical cord tape around the bowel.

Jejunostomies were performed to permit complete drainage of the stomach and duodenum. Although three methods were tried, none was entirely satisfactory. The principal difficulty was in obtaining free drainage with no back pressure as shown by duodenal distention.

The first method consisted of severing the intestine, tying off and inverting the aboral end, placing a small rubber tube in the proximal end and bringing it out through the abdominal wall.

The second method was similar except that no tube was used, and the wall of the intestine was sutured to the skin.

The third method was the most satisfactory and was done in two stages. Under ethylene anesthesia the upper jejunal loop was brought out through the muscles of the abdominal wall and the muscles approximated with the mesentery intervening. The skin was then sutured over the intestine. Several rabbits died of obstruction following this first stage, but some survived and were in good health. The second stage was done under infiltration with procaine hydrochloride. The skin was opened, the intestine severed and the aboral end tied off. Thus there was no soiling of the peritoneum and no change made in the position of the proximal end to interfere with complete drainage.

Gastrostomies were performed in conjunction with several obstructions. After completion of the obstruction, the stomach was sutured to each side of the abdominal incision over a distance of about 2 inches. The stomach was then opened and the mucous membrane sutured to the skin, thus permitting constant emptying of the stomach through the ventral abdominal wall.

Aspiration of stomach content by a catheter through the esophagus was found to be possible only when rabbits had been on an exclusive diet of lettuce, bread and water for from two to three weeks. After forty-eight hours' starvation the stomach was nearly empty, and the secretions accumulating after obstruction could be aspirated through a catheter.

Material to be put into the stomach after the intestine was obstructed was forced through a catheter.

Solutions of dextrose or sodium chloride were injected into the veins of the ear.

Blood for analysis was obtained from the veins of the ear or from the heart.

The nonprotein nitrogen of the blood was determined by the method of Folin and Wu.¹ The blood chlorides were determined by the method of Whitehorn.²

Blood for the determination of the alkali reserve was obtained from the heart and oxalated under oil. The method used was that of Van Slyke and Cullen,³ and Van Slyke.⁴

1. Folin, D., and Wu, H.: *J. Biol. Chem.* **38**:81, 1919.

2. Whitehorn, J. C.: *J. Biol. Chem.* **45**:449, 1921.

3. Van Slyke, D. D., and Cullen, G. E.: *J. Biol. Chem.* **30**:289, 1917.

4. Van Slyke: *J. Biol. Chem.* **30**:34, 1917.

The chlorides in the stomach and duodenal contents were determined in the following manner. A weighed portion of the stomach or intestinal contents was made distinctly alkaline with sodium carbonate, the mixture completely ashed, and the residue dissolved in distilled water containing nitric acid. In all, the equivalent of nitric acid was 5 cc. of a 1.42 specific gravity acid. From this point the procedure was the same as that for the determination of chlorides in the blood.

Some rabbits died from the obstruction sooner than was expected so that complete data on their blood were not obtained. Others contracted pneumonia soon after operation. Records of the experiments on such animals were discarded.

THE TOXICITY OF THE CONTENTS OF OBSTRUCTED INTESTINE

Rabbits vary considerably in the length of time they live after obstructions at similar points in their intestinal tracts. The amount of

TABLE 1.—*Changes in Blood Chlorides and Nonprotein Nitrogen Following Intestinal Obstruction at the Levels Indicated*

Rabbit	Before	12 Hr.	14 Hr.	20 Hr.	22 Hr.	24 Hr.	26 Hr.	39 Hr.	43 Hr.	49 Hr.	
3	Nonprotein nitrogen 54.5	..	111.0	Middle duodenum
	Chlorides..... 0.430	..	0.304	
2	Nonprotein nitrogen 82.1	224.5	Middle duodenum
	Chlorides..... 0.431	0.355	
10	Nonprotein nitrogen 44.4	78.9	Proximal jejunum
	Chlorides..... 0.495	0.460	
11	Nonprotein nitrogen 43.4	133.1	Proximal jejunum
	Chlorides..... 0.502	0.309	
18	Nonprotein nitrogen 32.4	120.0	Proximal jejunum
	Chlorides..... 0.393	0.346	
4	Nonprotein nitrogen 44.5	178.5	267.8	18 inches jejunum
	Chlorides..... 0.436	0.399	0.360	
8	Nonprotein nitrogen 39.5	214.3	..	Upper part of ileum
	Chlorides..... 0.482	0.339	..	
79	Nonprotein nitrogen 65.2	104.0	Terminal ileum
	Chlorides..... 0.475	0.420	
9	Nonprotein nitrogen 42.2	173.3	178.0	Terminal ileum
	Chlorides..... 0.455	0.419	?	
13	Nonprotein nitrogen 37.0	47.9	38.2	Operative manipulation
	Chlorides..... 0.466	0.461	0.471	
28	Nonprotein nitrogen 50.0	47.0	Starvation only
	Chlorides..... 0.507	0.498	

change in the nonprotein nitrogen and chlorides in the blood also varies somewhat, but as a rule is a dependable indication of the rabbit's condition. Obstruction in the middle of the duodenum is compatible with life for from fourteen to eighteen hours. Obstruction at the beginning of the jejunum caused death in from twenty-two to thirty hours. The duration of survival increases as the obstruction is lower so that life may last from eighty to two hundred hours when the obstruction is at the terminal ileum. These figures hold for rabbits receiving neither food nor water after the obstruction is created. Death occurs more rapidly if food or water is taken.

Contrary to some opinions, it will be noted that obstruction low in the small intestine causes as great a drop in blood chlorides as that fol-

lowing high obstruction, provided there is a proportionate increase in the duration of the obstruction. There is always an increase in the nonprotein nitrogen of the blood as well as in the alkali reserve.

When rabbits are nearing death from obstruction, there is a great decrease in body temperature. Blood pressure is low, and there is some concentration of blood as noted in the diminished amount of plasma in proportion to the cellular constituents. When the rabbits are sick, it is difficult and sometimes impossible to obtain blood from the veins of the ear, even after application of heat and xylol.

The release of an obstruction when the rabbit is nearing death induces a rapid change in its condition. Within an hour its body tem-

TABLE 2.—*Recovery After Release of Temporary Obstruction. The Time Intervals Tabulated Are Those After the Release of Obstruction*

Rab- bit	Re- Before lease	1 Hr.	2 Hr.	3 Hr.	3½ Hr.	4½ Hr.	6 Hr.	15 Hr.	1 Day	2 Days	3 Days	
	11 hr.											
3 N.P.N....	54.5	111.0	157.7	166.6	..	69.2	Middle
Chlorides	0.430	0.304	0.469	0.403	..	0.475	duodenum
	15 hr.											
7 N.P.N....	53.5	115.2	90.9	31.0	Middle
Chlorides	0.415	0.391	0.426	0.315	duodenum
	26 hr.											
19 N.P.N....	38.0	103.4	128.5	94.2	Proximal
Chlorides	0.389	0.346	0.485	0.452	jejunum
	24 hr.											
30 N.P.N....	39.0	103.8	..	86.3	Proximal
Chlorides	0.481	0.409	..	0.448	jejunum
	16 hr.											
5 N.P.N....	65.6	105.0	84.5	30.0	18 inches
Chlorides	0.468	0.402	0.485	0.498	jejunum
	22 hr.											
4 N.P.N....	44.5	267.8	215.9	176.5	44.9	18 inches
Chlorides	0.436	0.330	0.397	0.462	0.495	jejunum
	43 hr.											
8 N.P.N....	59.5	214.3	225.4	285.7	..	Upper part
Chlorides	0.482	0.339	0.403	0.425	..	of ileum
	43 hr.											
9 N.P.N....	42.2	178.6	132.2	Lower part
Chlorides	0.453	0.410	0.508	of ileum

perature has at least approached normal; it bleeds freely and hops around in apparent health. The blood chlorides are well on the way to normal by the end of an hour after release of the obstruction, and within three or four hours they are at or above the normal level. The nonprotein nitrogen of the blood drops soon after release if the rabbit has not been moribund, but when it has been near death the nonprotein nitrogen may increase for a time after the release before there is a return toward normal. The return of the nonprotein nitrogen to normal after release of low obstructions is not so rapid as that after the release of high obstructions.

The removal of the stomach contents before the release of the obstruction retards recovery. Substitution of an equivalent amount of distilled water, although presumably compensating for the loss of fluid,

does not hasten recovery. The blood chlorides remain low, and the nonprotein nitrogen remains elevated until food or water containing chlorides is given. Substitution of an equivalent amount of sodium chloride solution to compensate for the water and chloride removed from the stomach before release of the obstruction hastens recovery more than when distilled water is given but does not permit of rapid return

TABLE 3.—*The Effect on Recovery of Removing Stomach Contents Before Release of Obstruction at the Third Inch of the Jejunum. The Changes Are Noted When Solutions of Sodium Chloride or Hydrochloric Acid Are Substituted for the Stomach Contents Removed Before Release of Obstruction*

Rab- Wt., bit Lb.		Release Before 24 Hr.	2 Hr.	3 Hr.	18 Hr.	20 Hr.	42 Hr.	44 Hr.	
30	7½	N.P.N.... 39.0 Chlorides 0.481	103.8 0.409	86.3 0.448	Stomach contents not removed; obstruction released; neither food nor water until after last blood was taken
27	...	N.P.N.... 55.5 Chlorides 0.505	103.5 0.420	..	120.0 0.413	Stomach contents 153 Gm., 0.450 Gm. as sodium chloride. Stomach contents removed; obstruction released; neither food nor water until after last blood was taken
33	7¼	N.P.N.... 62.3 Chlorides 0.442	160.0 0.307	102.0 0.297	..	201.0 0.343	..	247.0 0.363	Stomach contents 155 Gm., 0.580 Gm. as sodium chloride. Stomach contents removed; obstruction released; distilled water given freely after release until 20 hr., then food
42	5	N.P.N.... 45.8 Chlorides 0.500	168.0 0.307	105.0 0.424	..	100.0 0.424	..	57.5 0.508	Stomach contents 160 Gm., 0.526 Gm. as sodium chloride. Stomach contents removed; obstruction released; 150 cc. water plus 0.6 Gm. sodium chloride given; distilled water 2 hr. after release, food 18 hr. after
41	7	N.P.N.... 46.0 Chlorides 0.500	116.2 0.370	107.0 0.439	..	100.0 0.508	Stomach contents 215 Gm., 0.704 Gm. as sodium chloride. Stomach contents removed; obstruction released; 150 cc. water plus hydrochloric acid equivalent to 0.6 Gm. sodium chloride given; distilled water 2 hr. after release, food 18 hr. after

of blood chlorides and nonprotein nitrogen to normal. Substitution of a solution of hydrochloric acid equivalent to the water and chlorides removed before release induces recovery almost as rapidly as that occurring after release of obstruction without removal of the stomach contents.

Rabbits having had their stomach contents removed before release of obstruction without replacement of chlorides by sodium chloride or hydrochloric acid do not appear entirely healthy. They bleed with

difficulty and are sluggish in their movements until they have been given food or water and their blood constituents return toward a normal level.

Comment.—The experimental observations reveal certain facts concerning intestinal obstruction, a few of which are new. They also justify explanations that may or may not be substantiated.

Rabbits die from obstruction of much shorter duration than do dogs. One rather obvious reason is that there is no vomiting and therefore no release of pressure in the obstructed bowel. Although rabbits do not vomit, the retained secretions are lost to the animal just as much as if vomiting had occurred. The amount of chloride in the contents of the obstructed bowel is sufficient to account for the fall in blood chlorides.

The higher the obstruction, up to the middle of the duodenum, the more rapid the death. It has been proved for rabbits and apparently holds true for dogs that the stomach and duodenum receive practically all the secretions entering the gastro-intestinal tract. These secretions come from the glands in the mucosa of the stomach and duodenum and also from the liver and pancreas.⁵ Loss of all the secretions entering the stomach and duodenum is incompatible with life. The lower the obstruction, the more reabsorption of these secretions, thus retarding dehydration as well as depleting the elements in blood going to form the secretions. During the first twenty-four hours of ileal obstruction there is almost no evidence of change in a rabbit's condition. The blood chloride, nonprotein nitrogen and alkali reserve differ but little from the normal. The animal appears healthy; it is warm and bleeds from its veins readily. During this first twenty-four hour interval reabsorption almost keeps pace with secretion. Since the entire intestinal tract is not available for absorption and none of the secreting portion is excluded, absorption lags behind secretion. Furthermore, as intrainestinal pressure is slowly increased, peristalsis is more vigorous, and secretion is accelerated. The increased amount of secretion augments intrainestinal pressure, giving rise to distention as the intestinal muscles lose their tone. As distention increases, absorption is proportionately retarded and is eventually almost nil. The changes in the blood during this period are great, and the change in the clinical picture is evident. All determinable deviations from normal are the same as those occurring in high obstruction but occur from twenty-four to forty-eight hours later.

In spite of apparent evidence to the contrary, it may be that toxemia plays a minor rôle in simple obstruction and that the real cause of death is the loss of secretions normally reabsorbed. The fact that extirpation of the duodenum has been found compatible with life need

5. Bunting and Jones: *J. Exper. Med.* **17**:192, 1913; **18**:25, 1913.

not alter this conception, for then there is no loss of secretions, the elements forming the secretions never being removed from the blood.

The release of temporary obstructions in rabbits, even when the animal is near death, permits return to health. The reabsorption of the contents of the obstructed bowel through normal intestine below the obstruction or from the obstructed bowel after the tension is lowered instead of showing evidence of the absorption of a noxious substance initiates a rapid return of the animal to normal. The blood chlorides are increased within one hour after release of the obstruction. This increase must be due to reabsorption, for the removal of the bowel contents above the obstruction prior to release does not permit an increase in the blood chlorides. This observation is further confirmation of the concept that the decrease in blood chlorides in obstruction is due solely to loss of stomach secretions. Furthermore, unless chlorides are given, the high nonprotein nitrogen shows no inclination to decrease. Some animals have lived for almost two days after release of jejunal obstructions with low blood chlorides and high nonprotein nitrogen and eventually recovered after the ingestion of food and water containing chlorides.

The removal of the stomach contents prior to release of temporary obstruction and the substitution of solutions of sodium chloride or hydrochloric acid in amounts comparable to the amount of water and chloride removed permit of recovery more rapidly than when distilled water is substituted but not so rapidly as when the obstruction is released without removal of the stomach contents. There are other elements in the secretions besides chlorides, the reabsorption of which benefits the animal.

THE EFFECTS OF DIMINISHED AND INCREASED INTRA- INTESTINAL PRESSURE

Attempts to reduce the intra-intestinal pressure in obstructed bowel were not uniformly successful and entailed additional operative trauma, which must be considered in interpreting results.

Jejunostomy, theoretically, causes only the entire loss of the secretions from the liver, pancreas and the gastro-intestinal mucosa above the segment opened. In the jejunostomies performed an element of partial obstruction was added in spite of efforts to prevent it, for none of the rabbits drained freely enough to obviate some duodenal distention. This presumably shortened the lives of the animals but does not entirely vitiate the observation that the length of life following jejunostomy is but little longer than that following obstruction at the same point. The changes in the blood are identical, and the appearance of the animal is the same.

Removal of the stomach contents every eight hours from an animal whose jejunum is obstructed relieves most of the excess intra-intestinal

pressure, although the duodenum is always moderately distended. This incomplete release of pressure in jejunal obstructions increases the time of survival from eight to fifteen hours.

Reducing intraduodenal pressure in jejunal obstruction by gastrostomy, done at the time the obstruction was created, adds a great deal of operative trauma but, even so, lengthens life from ten to fifteen hours.

The capacity of the stomach, or more likely the duodenum, to absorb water is much greater than has been supposed. Attempts to increase extra-intestinal pressure after obstruction of the jejunum by the introduction of water into the stomach in fairly large amounts were not

TABLE 4.—*The Effects of Reducing Intra-intestinal Pressure on Length of Life*

Rab-bit	Before	20 Hr.	24 Hr.	25½ Hr.	26 Hr.	30 Hr.	44 Hr.	46 Hr.	
10	N.P.N.... 44.4 Chlorides 0.495	78.9 0.460	Obstruction third inch of jejunum; not very sick at 20 hr.
25	N.P.N.... 48.7 Chlorides 0.487	111.5 0.349	Obstruction third inch of jejunum; fairly sick at 26 hours.
16	N.P.N.... 43.1 Chlorides 0.420	188.0 0.317	Jejunostomy third inch of jejunum; fairly sick; killed
74	N.P.N.... 36.2 Chlorides 0.439	..	109.2 0.401	154.0 0.396	Obstruction third inch of jejunum; stomach contents removed 8, 16 and 24 hours after obstruction; fairly sick; killed at 30 hours
94	N.P.N.... 40.5 Chlorides 0.462	..	58.0 0.462	48.7 0.479	Stomach sutured to anterior belly wall as control; lived
96	N.P.N.... 50.0 Chlorides 0.420	..	103.6 0.366	243.9 0.257	..	Pyloric obstruction and gastrostomy permitting complete emptying of stomach; dying at 44 hours
92	N.P.N.... 46.1 Chlorides 0.515	..	152.6 0.469	Obstruction third inch of jejunum and gastrostomy permitting complete emptying of stomach; died at 33 hours

successful. The excess water was readily absorbed, for when the animal was killed, there were but little more stomach and duodenal contents than are found in rabbits of the same size after simple obstruction. This work was done during hot weather which probably influenced the results.

The introduction of liquid albolene into the stomach after obstruction of the jejunum gave different results. Since there was no absorption of albolene, intra-intestinal pressure was increased immediately, and death occurred from eight to ten hours sooner than it does after simple obstruction. There was also an increased amount of stomach and duodenal contents, rabbits so treated having about the same amount (albolene discarded) at their death in twenty hours as those with simple obstruction had in from twenty-six to thirty hours. The amount of chlorides in the stomach contents was virtually the same in the two groups.

Increasing intra-intestinal pressure after jejunal obstruction by the introduction into the stomach of stomach and duodenal contents, obtained after twenty-six hours of jejunal obstruction in another animal, shortened the usual length of life and caused a greater increase in the nonprotein nitrogen of the blood than that observed after using albolene.

Since the duration of life is longer after ileal obstruction, increments in intra-intestinal pressure make differences in the time of survival more

TABLE 5.—*The Effects of Increasing Intra-intestinal Pressure in Animals Obstructed at the Third Inch of the Jejunum. The Pressure Was Increased by Giving Water, Liquid Albolene or the Stomach Contents of a Rabbit Having Had a Jejunal Obstruction for Twenty-Six Hours Through a Catheter Passed into the Stomach*

Rab- bit	Before	10 Hr.	20 Hr.	22 Hr.	24 Hr.	30 Hr.	
10	Nonprotein nitrogen 44.4	..	78.9	Obstructed third inch of jejunum;
	Chlorides..... 0.495	..	0.460	not very sick
27	Nonprotein nitrogen 55.5	103.5	..	Obstructed third inch of jejunum;
	Chlorides..... 0.505	0.420	..	fairly sick
64	Nonprotein nitrogen 48.0	77.7	..	Obstructed third inch of jejunum;
	Chlorides..... 0.515	0.363	..	100 cc. water immediately; not
76	Nonprotein nitrogen 39.9	129.8	157.3	Obstructed third inch of jejunum;
	Chlorides..... 0.427	0.391	0.349	100 cc. water immediately, 100 cc.
							in 8 hours, 75 cc. in 24 hours;
85	Nonprotein nitrogen 53.7	122.0	very sick; killed in 30 hours
	Chlorides..... 0.467	0.430	Obstructed third inch of jejunum;
77	Nonprotein nitrogen 58.8	200.0	120 cc. albolene immediately;
	Chlorides..... 0.502	0.346	fairly sick; killed in 22 hours
							Obstructed third inch of jejunum;
86	Nonprotein nitrogen 49.6	177.0	100 cc. albolene immediately,
	Chlorides..... 0.512	0.429	100 cc. in 7 hours; dying, killed
							in 19 hours
87	Nonprotein nitrogen 60.0	203.0	Obstructed third inch of jejunum;
	Chlorides..... 0.508	0.430	120 cc. stomach contents im-
							mediately; fairly sick; killed in 22
							hours

apparent. The capacity of the small intestine for the absorption of water is great. Rather large amounts of water introduced into the stomach at short intervals following obstruction at the terminal ileum caused no appreciable increase in intra-intestinal pressure and did the animals no harm. The work was done during hot weather which probably affected the results.

Increasing intra-intestinal pressure by the introduction of liquid albolene into the stomach after obstruction at the terminal ileum shortens life materially. The animals die with as great changes in their blood chlorides and nonprotein nitrogen after the same duration of obstruction as those having high jejunal obstructions.

The effects of the introduction of stomach and duodenal contents, obtained from an animal having jejunal obstruction for twenty-six hours, into the stomach of a rabbit immediately following obstruction at the terminal ileum are not great. The animals are but little more distended at the end of twenty-four hours than are those having simple ileal obstruction, and the deviations of their blood chlorides and non-protein nitrogen from the normal are not much greater.

Comment.—Reducing the pressure that develops within the bowel above the level of the induced obstruction increases the duration of survival and restricts correspondingly the alterations in blood chlorides

TABLE 6.—*The Effects of Increasing Intra-intestinal Pressure in Rabbits Obstructed at the Terminal Ileum. The Pressure was Increased by Giving Water, Liquid Albolene or the Stomach Contents of a Rabbit Having Had a Jejunal Obstruction for Twenty-Six Hours, Through a Catheter Passed into the Stomach*

Rab- bit		Before	22½ Hr.	24 Hr.	43 Hr.	
9	Nonprotein nitrogen	42.2	173.3	Ileal obstruction; fairly sick
	Chlorides.....	0.455	0.419	
63	Nonprotein nitrogen	39.2	..	52.2	..	Ileal obstruction; 100 cc. water immediately; not sick
	Chlorides.....	0.521	..	0.452	..	
69	Nonprotein nitrogen	46.8	..	70.0	..	Ileal obstruction; 100 cc. water immediately and at 2, 4 and 6 hours; not much distention; not sick
	Chlorides.....	0.500	..	0.372	..	
89	Nonprotein nitrogen	48.3	166.6	Ileal obstruction; 180 cc. albolene immediately, 100 cc. in 8 hours; enormous distention; dying in 22½ hours
	Chlorides.....	0.508	0.369	
91	Nonprotein nitrogen	50.1	157.7	Ileal obstruction; 180 cc. albolene immediately, 100 cc. in 8 hours; very sick; greatly distended; killed in 22½ hours
	Chlorides.....	0.512	0.438	
90	Nonprotein nitrogen	46.1	87.3	Ileal obstruction; 180 cc. stomach contents immediately, 100 cc. in 6 hours; moderately sick; moderately distended; killed in 22½ hours
	Chlorides.....	0.495	0.475	
103	Nonprotein nitrogen	46.0	116.0	Ileal obstruction; 180 cc. stomach contents immediately, 100 cc. in 5 hours; not very sick; not much distention; killed in 22½ hours
	Chlorides.....	0.475	0.424	

and nonprotein nitrogen. The reasons are definite. As intra-intestinal pressure rises above normal, hyperperistalsis is provoked and continues until the increasing fatigue of the muscularis results in corresponding grades of distention. The rate of secretion is in general directly proportional to the activity of peristalsis. The rate of absorption is inversely proportional to the degree of distention. Thus it follows that increasing intra-intestinal pressure provokes hyperperistalsis which in turn stimulates secretion; the resulting distention diminishes the capacity for reabsorption of these secretions.

The following observation is illustrative. Obstruction of the jejunum was made in the same manner in rabbits of the same size and continued for twenty-six hours. If the stomach contents are removed by aspiration

every eight hours, the total amount obtained is less than when the contents are allowed to collect under increasing pressure for the full period of the obstruction. Longer life after obstruction and restricted alterations in blood chlorides and nonprotein nitrogen provided by reducing intra-intestinal pressure cannot be the result of a decreased absorption of a toxic substance from the lumen of the bowel. The rate of absorption is augmented by reducing tension, and, if an absorbable toxic substance is present, life would be shortened and the symptoms of intoxication would be intensified. Available evidence indicates that survival is longer when intra-intestinal pressure is reduced because there is not so great a loss of the constituents forming the secretions that enter the stomach and duodenum.

The increase of intra-intestinal pressure in jejunal obstruction induced by the introduction of 120 cc. of albolene into the stomach stimulates secretion and retards reabsorption. Blood chlorides are just as low at the end of nineteen hours as they are after twenty-six hours when the pressure is not thus increased. The distention in itself is not the cause of early death, for these animals are greatly distended immediately after obstruction. They seem perfectly healthy until a few hours before death when the typical lethal symptoms develop.

The greater deviation from the normal level of the nonprotein nitrogen of the blood noted after increasing intra-intestinal pressure by introducing 120 cc. of the contents of obstructed bowel from another animal is difficult to explain. Clinically, these animals appeared no worse than those given albolene. It is possible that a larger series would show different results. The only plausible explanations are the presence of a noxious product in the stomach and duodenal contents introduced or that the contents introduced are sufficiently irritating to stimulate secretion more than does albolene.

The untoward effect of increasing intra-intestinal pressure following obstruction at the terminal ileum is evident. When pressure is not increased, there is an interval of about twenty-four hours in the animals with low obstructions before reabsorption lags too far behind secretion. The introduction of liquid albolene immediately after the obstruction is produced seems almost entirely to inhibit reabsorption as well as indirectly to stimulate secretion so that the animals die almost as quickly as do those having duodenal obstructions. The fact that the blood chlorides and nonprotein nitrogen are approximately the same as those found after the same duration of duodenal obstruction makes it evident that death is not due solely to distention. Furthermore, even though greatly distended immediately after obstruction, they appear to be healthy until a few hours before death.

The effects of increasing intra-intestinal pressure following obstructions at the terminal ileum by introducing contents of obstructed bowel into the stomach are not great. Death occurs little sooner than it

does following simple ileal obstruction. At the end of twenty-four hours, the changes of the blood chloride and of the nonprotein nitrogen from the normal are not marked. There is little distention, since the water in the obstructed contents is absorbed.

The difference in the effect produced by introducing the stomach and duodenal contents into the stomach to increase pressure in jejunal and ileal obstructions may be explained by the rapid descent of the contents in ileal obstruction to the jejunum and ileum where they cannot stimulate secretion by irritation of the stomach and duodenal mucosa.

TABLE 7—*The Therapeutic Value of Solutions of Sodium Chloride as Compared to Dextrose Given Intravenously When Intra-intestinal Pressure Is Not Diminished Stomach and Duodenal Contents Removed After Death and Analyzed for Chloride Content*

Rab- Wt, bit	Lb		Before	20 Hr	24 Hr	26 Hr	
71	4½	Nonprotein nitrogen	41.3		152.6	.	Obstructed third inch jejunum
		Chlorides	0.488		0.420		
		Alkali reserve	.		69.0		
78	4½	Nonprotein nitrogen	38.9		142.0	.	Obstructed third inch jejunum, con-
		Chlorides	0.488		0.396		tents of obstructed bowel, 222 Gm,
							0.741 Gm as sodium chloride
58	5½	Nonprotein nitrogen	42.5	152.6	.	.	Obstructed third inch jejunum, 40 cc
		Chlorides	0.528	0.380	.	.	5 per cent dextrose at 8 and 16 hours
		Alkali reserve		65.5			after obstruction
59	6	Nonprotein nitrogen	48.7	132.4		..	Obstruction third inch jejunum, 40 cc
		Chlorides	..	0.503	0.538		0.9 per cent sodium chloride at 8
		Alkali reserve		58.0			and 16 hours after obstruction
46	4½	Nonprotein nitrogen	38.0			125.3	Obstructed third inch jejunum, 40 cc
		Chlorides	0.475			0.353	5 per cent dextrose at 8 and 16 hours
							after obstruction, contents of ob-
							structed bowel 278 Gm, 0.884 Gm
							as sodium chloride
47	3¾	Nonprotein nitrogen	53.0			124.5	Obstructed third inch jejunum, 40 cc
		Chlorides	0.473			0.538	0.9 per cent sodium chloride at 8
							and 16 hours after obstruction; con-
							tents of obstructed bowel 251 Gm,
							1.082 Gm as sodium chloride

THE THERAPEUTIC VALUE OF SOLUTIONS OF SODIUM CHLORIDE

The intravenous administration of solutions of 5 per cent dextrose or of 0.9 per cent sodium chloride every eight hours after jejunal obstruction lengthens the life of rabbits from two to six hours. There seems to be no difference between the effects of the two solutions as far as survival is concerned. There is with both an increase in the amount of distention due primarily to increased secretion and finally to diminished absorption as distention progresses. The partial correction of the developing dehydration enables the glands of the mucosa to secrete more than when no fluids are given. The harmful effects of the increased intra-intestinal pressure are a little more than offset by the beneficial effects of diminished dehydration. Solutions of sodium chloride seem to have no specific curative effect. The loss of chlorides into the contents

of the obstructed bowel is compensated for by that given intravenously, but the nonprotein nitrogen increases almost as much as when solutions of dextrose are given.

When intra-intestinal pressure is reduced by aspiration or gastrostomy or when all secretions are lost with a jejunostomy, the therapeutic value of solutions of sodium chloride given intravenously or

TABLE 8.—*The Therapeutic Value of Solutions of Sodium Chloride as Compared to Dextrose Given Intravenously When Intra-intestinal Pressure Is Reduced by the Methods Indicated. The Stomach Contents Were Removed Through a Catheter Passed into the Stomach*

Rab- bit	Wt., Lb.	Before	24 Hr.	28 Hr.	30 Hr.	36 Hr.	37 Hr.	38 Hr.	47 Hr.	48 Hr.	67 Hr.	
74	4½	Obstructed third inch jejunum; stomach contents removed 8, 16, 24 and 30 hours after obstruction
N.P.N....	36.2	109.2	..	154.0	
Chlorides	0.439	0.401	..	0.396	
36	4¾	Died	Obstructed third inch jejunum; 40 cc. 0.9 per cent sodium chloride 8, 16, 24 and 32 hours after obstruction; stomach contents removed 8, 16, 24 and 32 hours after obstruction
N.P.N....	40.0	104.0	
Chlorides	0.491	0.479	
43	Died	Jejunostomy; 40 cc. 0.9 per cent sodium chloride 8 and 16 hours after operation; partial obstruction
N.P.N....	53.0	96.6	
Chlorides	0.496	0.545	
44	Dying	Jejunostomy; 40 cc. 5 per cent dextrose 8 and 16 hours after operation
N.P.N....	58.8	148.8	274.0	
Chlorides	0.512	0.429	0.375	
82	Dying	Jejunostomy, 2 stage; 40 cc. 0.9 per cent sodium chloride 8, 16, 24, 32 and 40 hours after operation
N.P.N....	58.8	112.3	224.3	
Chlorides	0.508	0.578	0.548	
93	Dying	Obstructed third inch jejunum; gastrostomy; 40 cc. 2.5 per cent dextrose 8, 16, 24 and 32 hours after obstruction
N.P.N....	44.0	157.4	208.3	
Chlorides	0.459	0.452	0.376	
98	Dying	Pyloric obstruction; gastrostomy; 40 cc. 2.5 per cent dextrose 7, 13 and 23 hours after obstruction
N.P.N....	46.8	..	240.9	
Chlorides	0.402	..	0.370	
101	Dying	Pyloric obstruction; gas-
N.P.N....	45.4	145.9	229.8	..	trostomy; 40 cc. 0.9 per
Chlorides	0.488	0.393	0.343	..	cent sodium chloride 7, 13, 23, 30, 35, 46, 52 and 58 hours after obstruction

subcutaneously becomes evident. Life is prolonged from twelve to sixteen hours by the administration of sodium chloride solution at short intervals if the stomach contents are removed every eight hours from an animal with jejunal obstruction. There is less increase in the non-protein nitrogen in the blood than when solutions of dextrose are given.

The difference in value between the two solutions is evident when they are given to animals on which a jejunostomy has been performed.

The duration of life is shorter, and the nonprotein nitrogen is higher when dextrose is administered than when saline is used.

Reduction of intra-intestinal pressure in jejunal obstruction by means of gastrostomy adds considerable operative trauma so that the results are undeterminate. Presumably life would have been prolonged considerably beyond the actual time noted if this trauma had not been added.

The difference of twenty hours in the length of survival of animals suffering loss of both stomach and duodenal secretions as found in those having a jejunostomy, and a loss of only stomach secretions as seen in pyloric obstruction with gastrostomy is evidence that the loss of duodenal secretions is not compensated for by saline. This differ-

TABLE 9.—*The Effect of Intravenous Administration of the Solutions Indicated on the Alkali Reserve and Nonprotein Nitrogen of Blood*

Rab. Wt., bit Lb. Before	Hr.	24		
56	5	Normal animal.....	Starved 24 hours; water given freely
		Alkali reserve.....	.. 56.4	
52	5½	Nonprotein nitrogen	37.0 41.0	Starved 72 hours; water given freely; given 30 cc.
		Chlorides.....	0.492 0.467	2.5 per cent dextrose in vein at beginning of
		Alkali reserve.....	.. 61.4	experiment and again 10 hours later; rabbit bled
				from heart and killed in 24 hours; distilled water
				given freely
53	4%	Nonprotein nitrogen	32.0 42.0	Starved 72 hours; water given freely; given 20 cc.
		Chlorides.....	0.479 0.462	3 per cent sodium bicarbonate neutralized with
		Alkali reserve.....	.. 65.4	lactic acid in vein at beginning of experiment
				and again 10 hours later; rabbit bled from heart
				and killed in 24 hours; distilled water given freely
54	5½	Nonprotein nitrogen	35.7 46.5	Starved 72 hours; water given freely; given 20 cc.
		Chlorides.....	0.492 0.465	1 per cent lactic acid in vein at beginning of
		Alkali reserve.....	.. 54.0	experiment and again 10 hours later; rabbit bled
				from heart and killed in 24 hours; distilled water
				given freely
50	2½	Nonprotein nitrogen	33.5 62.8	No starvation; given 20 cc. 3 per cent sodium
		Chlorides.....	0.462 0.412	bicarbonate in vein at beginning of experiment
		Alkali reserve.....	.. 95.0	and again 10 hours later; rabbit bled from heart
				and killed in 24 hours; distilled water given freely

ence in survival would probably have been still greater had sufficient sodium chloride been given the animal with pyloric obstruction to maintain the blood chloride at the normal level.

The intravenous administration of solutions of dextrose or of sodium bicarbonate neutralized with lactic acid caused no appreciable changes in the alkali reserve or nonprotein nitrogen of a healthy rabbit.

Sufficient lactic acid to produce noticeable changes in the alkali reserve could not be given without immediately killing the animal.

Solutions of sodium bicarbonate given intravenously in sufficient quantity materially to increase the alkali reserve caused a great increase in the nonprotein nitrogen of the blood.

Comment.—The therapeutic value of the intravenous or subcutaneous administration of solutions of sodium chloride increases as

intra-intestinal pressure is diminished and, conversely, the value decreases as intra-intestinal pressure is increased. The increased supply of fluid enables the animal to increase its gastric and duodenal secretions, thus augmenting distention and diminishing reabsorption unless means are employed to reduce intra-intestinal pressure. The value of sodium chloride lies in the establishment of a normal blood chloride level which corrects alkalosis and thereby lowers the high nonprotein nitrogen.

Life is prolonged most by sodium chloride in pyloric obstructions when gastric distention is prevented by gastrostomy. Here there is loss of gastric secretions of which the chloride is the most important constituent. Replacement of this chloride loss would presumably permit of survival until starvation occurred were it not for the operative trauma. Continued removal of accumulated secretions in the stomach from rabbits with jejunal obstruction and the administration of sodium chloride solutions almost doubles the length of life of rabbits as compared with those having simple jejunal obstruction.

The kidneys show little damage from intestinal obstruction. There is an increased output of urea in the urine during intestinal obstruction as well as the increase in the blood urea.⁶ Evidently catabolic processes are forming waste products more rapidly than normal and more rapidly than the kidney can excrete the accumulating urea. The diminished chlorides may be the cause of this increased catabolism. Presumably there is no appreciable damage to the kidney following twenty-four hour alkalosis induced by the intravenous administration of sodium bicarbonate. The increased nonprotein nitrogen in the blood must then be accounted for by increased catabolism or by abnormal metabolism. The alkalosis accompanying intestinal obstruction may be the cause of part of the increase found in the nonprotein nitrogen. Such an explanation accounts for the rapid decrease in the nonprotein nitrogen found when solutions of sodium chloride are given to correct the alkalosis.

CLINICAL APPLICATION

Rabbits differ from human beings in many respects; nevertheless, certain conclusions seem warranted.

The administration of isotonic or slightly hypertonic solutions of sodium chloride is of great value when measures are taken to insure the least possible increase above the normal intra-intestinal pressure. These measures include the release of the obstruction. The intestinal musculature in human beings does not regain its tone after distention so rapidly as in rabbits, so that simply releasing the obstruction may not reduce intra-intestinal pressure. When the obstruction is high, gastric lavage may diminish pressure sufficiently to restore muscle tone.

6. Haden, R. L., and Orr, T. G.: *Bull. Johns Hopkins Hosp.* 34:26, 1923.

When a large part of the intestine is distended, it must be emptied, preferably by a method causing the least trauma. The intestinal contents need not be removed because of their toxicity, but they must be expelled to relieve pressure. In some instances the intravenous administration of 25 per cent sodium chloride will stimulate peristalsis sufficiently to induce propulsion of intestinal contents and relieve undue pressure. It may be necessary to remove the contents mechanically as by aspiration with trocars at numerous levels. This procedure, in spite of all precautions, is likely to soil the peritoneal cavity and is accompanied by the deleterious effects of trauma. A jejunostomy may be done, not to drain away all the secretions, but to relieve pressure sufficiently to permit of reabsorption of secretions. When intrainestinal pressure is low or has been reduced, it can be kept low by measures that diminish secretion. Large doses of morphine inhibit peristalsis and diminish secretion and thereby aid materially in keeping intra-intestinal pressure low. Such measures will insure the greatest amount of reabsorption of secretions, and thus will aid materially in promoting recovery.

Peritonitis is, in most instances, more dangerous because of the accompanying intestinal paresis than because of the toxicity of infection. Similar methods of treatment are applicable. When there is little distention, the withholding of nourishment by the mouth diminishes secretion. Morphine in liberal doses further decreases secretion so that the limited capacity for absorption is not overtaxed. Solutions of sodium chloride and of dextrose given intravenously restore any deficiency of blood chlorides to normal as well as supply nourishment.

When there is considerable distention, jejunostomy will aid in reducing intra-intestinal pressure. The jejunostomy should be done so as to relieve excess pressure but not to afford complete drainage of gastric and duodenal secretions, for such complete drainage is as disastrous as continued paresis.

SUMMARY

1. Rabbits recover more rapidly from intestinal obstruction if they are permitted to reabsorb the contents of obstructed intestine than when such contents are removed.
2. Diminishing intra-intestinal pressure in obstructed bowel prolongs the life of rabbits, because it diminishes secretions and promotes reabsorption.
3. Increasing the intra-intestinal pressure in obstructed bowel shortens the life of rabbits, because it stimulates secretion and diminishes reabsorption.
4. The therapeutic value of solutions of sodium chloride increases as intra-intestinal pressure in the obstructed bowel diminishes, and, conversely, the value diminishes as intra-intestinal pressure increases.

PROTOCOLS. PART I

Rabbit 1—Duodenal obstruction—1/21/27. General diet: No food for 48 hours; water ad lib				
	Before Obstruction	24 Hours after Obstruction	48 Hours after Obstruction	
Nonprotein nitrogen	53.5	50.5	50	
Chlorides	0.353	0.370	0.383	

Ethylene anesthesia 10 minutes. Obstruction, rubber band, middle duodenum. Blood from ear. Water ad lib postoperatively. Killed after 48 hours. Obstruction not complete.

Rabbit 2—Duodenal obstruction—1/21/27. General diet: No food for 48 hours; water ad lib.				
	Before Obstruction	12 Hours after Obstruction	5 Hours after Release	
Nonprotein nitrogen ...	52.1	221.5	242	
Chlorides	0.413	0.355	0.424	

Ethylene anesthesia 12 minutes. Obstruction, rubber band, middle duodenum. Blood from ear. Bled with difficulty after 12 hours. Rabbit cold. Obstruction released in 12 hours. Water ad lib postoperatively. Food 5 hours after release at which time rabbit seemed perfectly healthy. Living and apparently healthy 1 week later.

Rabbit 3—Duodenal obstruction—1/31/27. General diet: No food for 48 hours; water ad lib				
	Before Obstruction	14 Hours After Obstruction	4½ Hours After Release	29 Hours After Release
Nonprotein nitrogen	54.5	111	157.7	166.6
Chlorides	0.430	0.304	0.469	0.403

Ethylene anesthesia 12 minutes. Obstruction, rubber band, middle duodenum. Blood from ear. Obstruction released after 14 hours at which time rabbit was bled with difficulty. Water ad lib postoperatively. Food 4½ hours after release at which time rabbit appeared perfectly healthy. Living and apparently healthy 1 week later.

Rabbit 4—Jejunal obstruction—1/31/27. General diet: No food for 48 hours; water ad lib				
	Before Obstruction	22 Hours After Obstruction	29 Hours After Release	3½ Hours After Release
Nonprotein nitrogen....	44.5	178.5	267.8	245.9
Chlorides	0.436	0.399	0.360	0.397

Ethylene anesthesia 10 minutes. Obstruction, rubber band, 18 inches below beginning of jejunum. Blood from ear. Obstruction released after 29 hours. Water ad lib postoperatively. Food 3½ hours after release. Living and apparently healthy 1 week later.

Rabbit 5—Jejunal obstruction—2/7/27. General diet: No food for 48 hours; water ad lib				
	Before Obstruction	16 Hours After Obstruction	1 Hour After Release	24 Hours After Release
Nonprotein nitrogen. ...	66.6	105	84.5	30
Chlorides	0.468	0.462	0.485	0.498

Ethylene anesthesia 10 minutes. Obstruction, rubber band, 18 inches below beginning of jejunum. Blood from ear. Obstruction released in 16 hours. Water ad lib postoperatively. Food 1 hour after release. Living and apparently healthy 1 week later.

Rabbit 6—Jejunal obstruction—2/7/27. General diet: No food for 48 hours; water ad lib				
	Before Obstruction	16 Hours After Obstruction	2 Hours After Release	
Nonprotein nitrogen ..	42.9	137.9	115.4	
Chlorides	0.482	0.405	0.482	

Ethylene anesthesia 10 minutes. Obstruction, rubber band, 18 inches below beginning of jejunum. Blood from ear. Obstruction released in 16 hours. Water ad lib postoperatively. Food 2 hours after release. Living and apparently healthy 1 week later.

Rabbit 7—Jejunal obstruction—2/7/27. General diet: No food for 48 hours; water ad lib				
	Before Obstruction	15 Hours After Obstruction	3 Hours After Release	24 Hours After Release
Nonprotein nitrogen ..	53.5	115.2	90.9	31
Chlorides	0.415	0.391	0.426	0.515

Ethylene anesthesia 10 minutes. Obstruction, rubber band, 18 inches below beginning of jejunum. Blood from ear. Obstruction released in 15 hours. Water ad lib postoperatively. Food 3 hours after release. Living and apparently healthy 1 week later.

Rabbit 8—Ileal obstruction—2/24/27. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	43 Hours After Obstruction	6 Hours After Release	2 Days After Release
Nonprotein nitrogen.....	39.5	214.3	225.4	225.7
Chlorides	0.452	0.339	0.403	0.426

Ethylene anesthesia 8 minutes. Obstruction, rubber band, upper ileum. Blood from ear. Obstruction released in 43 hours. Water ad lib postoperatively. Food 6 hours after release. Rabbit died 4 days after obstruction from pneumonia.

Rabbit 9—Ileal obstruction—2/24/27. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	43 Hours After Obstruction	49 Hours After Obstruction	2 Days After Release
Nonprotein nitrogen	42.2	173.3	178.6	138.2
Chlorides	0.455	0.419	0.508

Ethylene anesthesia 8 minutes. Obstruction, rubber band, terminal ileum. Blood from ear. Obstruction released in 49 hours. Water ad lib postoperatively. Food immediately after release. Rabbit died 1 week after release from adhesions producing partial intestinal obstruction.

Rabbit 10—Jejunal obstruction—3/8/27. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	20 Hours After Obstruction	5 Hours After Release	40 Hours After Release
Nonprotein nitrogen.....	44.4	78.9	123.7	39.6
Chlorides	0.495	0.460	0.475	0.532

Ethylene anesthesia 10 minutes. Obstruction, rubber band, third inch jejunum. Blood from ear. Obstruction released in 20 hours. Water ad lib postoperatively. Food 5 hours after release. Living and apparently healthy 1 week later.

Rabbit 11—Jejunal obstruction—3/8/27. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction
Nonprotein nitrogen	43.4	133.1
Chlorides	0.502	0.409

Ethylene anesthesia 10 minutes. Obstruction, rubber band, third inch jejunum. Blood from ear. Obstruction released in 24 hours. Water ad lib postoperatively. Food immediately after release. Living and apparently healthy 1 week later.

Rabbit 13—Control operation—3/29/27. General diet: No food for 48 hours; water ad lib.

	Before Operation	22 Hours After Operation	49 Hours After Operation
Nonprotein nitrogen	37	47.9	38.2
Chlorides	0.466	0.461	0.471

Ethylene anesthesia 10 minutes. Abdomen was opened, intestines drawn out of abdominal cavity and replaced. There was considerably more manipulation of the intestines than usually occurs in producing obstruction. Blood from ear. Rabbit made an uneventful recovery.

Rabbit 14—Jejunal obstruction—11/1/27. Weight 4½ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction
Nonprotein nitrogen	44.1	122.4
Chlorides	0.432	0.376

Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
Stomach and duodenal.....	157.8	0.206	0.325

Ethylene anesthesia 10 minutes. Obstruction, umbilical tape, third inch jejunum. Blood from ear. Rabbit killed 24 hours after obstruction. Neither food nor water postoperatively. There were no signs of severe toxemia. Stomach and duodenal contents removed.

Rabbit 15—Jejunal obstruction—11/1/27. Weight 3½ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction
Nonprotein nitrogen	48.3	145.1
Chlorides	0.429	0.370

Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
Stomach and duodenal.....	191.7	0.249	0.479

Ethylene anesthesia 5 minutes. Obstruction, umbilical tape, third inch jejunum. Blood from ear. Rabbit killed in 24 hours. Neither food nor water postoperatively. No signs of severe toxemia. Stomach and duodenal contents removed.

Rabbit 18—Jejunal obstruction—11/21/27. Weight $4\frac{1}{2}$ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	26 Hours After Obstruction
Nonprotein nitrogen	32.4	120
Chlorides	0.393	0.346

Ethylene anesthesia 12 minutes. Obstruction, umbilical tape, third inch jejunum. Blood from ear. Rabbit killed in 26 hours after obstruction. Neither food nor water postoperatively.

Rabbit 19—Jejunal obstruction—11/21/27. Weight $4\frac{1}{4}$ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	26 Hours After Obstruction	1 Hour After Release	24 Hours After Release
Nonprotein nitrogen.....	38	103.4	123.5	91.2
Chlorides	0.389	0.316	0.485	0.453

Ethylene anesthesia 15 minutes. Obstruction, rubber band, third inch jejunum. Blood from ear. Obstruction released in 26 hours. Neither food nor water postoperatively, until 24 hours after release. Living and apparently healthy 1 week later.

Rabbit 20—Control—12/12/27. Weight $5\frac{1}{4}$ pounds. General diet: No food for 48 hours; water ad lib.

Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
Stomach and duodenal.....	153.5	0.310	0.476
Intestinal	117.5	0.060	0.071

Normal rabbit killed. Stomach and duodenal contents removed. Small and large intestinal contents removed.

Rabbit 21—Jejunal obstruction—12/20/27. Weight $4\frac{1}{2}$ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	26 Hours After Obstruction	2 Hours After Release	21 Hours After Release
Nonprotein nitrogen ..	51.8	186.2	180.7	187
Chlorides	0.436	0.435	0.410	0.485

Ethylene anesthesia 15 minutes. Obstruction, rubber band, third inch jejunum. Blood from ear. Obstruction released in 26 hours. Neither food nor water postoperatively until 2 hours after release. Living and apparently healthy 1 week later.

Rabbit 22—Jejunal obstruction—12/20/27. Weight $5\frac{1}{4}$ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	26 Hours After Obstruction	Per Cent as NaCl	Total as NaCl, Gm.
Nonprotein nitrogen ...	48.7	213.4		
Chlorides	0.446	0.420		

Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
Stomach and duodenal.....	192	0.212	0.407
Intestinal	60	0.156	0.105

Ethylene anesthesia 15 minutes. Obstruction, rubber band, third inch jejunum. First blood from ear. Second from heart. Rabbit too sick to bleed at 26 hours. Killed and blood taken from heart. Stomach and duodenal contents removed. Small and large duodenal contents removed. Neither food nor water postoperatively. A great deal of gas in stomach and duodenum causing enormous distention.

Rabbit 23—Control—12/28/27. General diet.

Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
Stomach and duodenal.....	139	0.457	0.635
Intestinal	61.5	0.045	0.025

Normal rabbit killed after regular feeding. Stomach and duodenal contents removed. Small and large intestinal contents removed.

Rabbit 24—Jejunal obstruction—2/9/28. Lettuce and bread diet 2 weeks: No food for 48 hours; water ad lib.

	Before Obstruction	26 Hours After Obstruction	1½ Hours After Release
Nonprotein nitrogen.....	46.1	109.5	145
Chlorides	0.408	0.248	0.211

Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
Stomach	168	0.239	0.402

Ethylene anesthesia 10 minutes. Obstruction, rubber band, third inch jejunum. Blood from ear. Stomach contents removed by catheter through esophagus 26 hours after obstruction. Obstruction released. Neither food nor water postoperatively until 1½ hours after release. Living and apparently healthy 1 week later.

Rabbit 25—Jejunal obstruction—2/9/28. Lettuce and bread diet 2 weeks: No food for 48 hours; water ad lib.

	Before Obstruction	26 Hours After Obstruction
Nonprotein nitrogen...	48.7	111.5
Chlorides	0.487	0.349

Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
Stomach	153	0.193	0.3003

Ethylene anesthesia 10 minutes. Obstruction, rubber band, third inch jejunum. Blood from ear. Stomach contents removed by catheter through esophagus 26 hours after obstruction. Obstruction released. Neither food nor water postoperatively until release of obstruction. Living and apparently healthy 1 week later.

Rabbit 26—Jejunal obstruction—2/16/28. Lettuce and bread diet 3 weeks: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	2 Hours After Release
Nonprotein nitrogen.....	61.8	128.8	135.3
Chlorides	0.468	0.445	0.376

Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
Stomach	125.5	0.342	0.430

Ethylene anesthesia 10 minutes. Obstruction, rubber band, third inch jejunum. Blood from ear. Stomach contents removed by catheter through esophagus 24 hours after obstruction. Obstruction released. Neither food nor water postoperatively until 2 hours after release. Living and apparently healthy 1 week later.

Rabbit 27—Jejunal obstruction—2/16/28. Lettuce and bread diet 3 weeks: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	3 Hours After Release
Nonprotein nitrogen	55.5	103.5	120
Chlorides	0.505	0.420	0.413

Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
Stomach	153	0.294	0.450

Ethylene anesthesia 10 minutes. Obstruction, rubber band, third inch jejunum. Blood from ear. Stomach contents removed by catheter through esophagus 24 hours after obstruction. Obstruction released. Neither food nor water postoperatively until 3 hours after release. Living and apparently well 1 week later.

Rabbit 28—Control—2/16/28. Lettuce and bread diet 3 weeks: No food for 48 hours; water ad lib.

	At 48 Hours Starvation	At 72 Hours Starvation
Nonprotein nitrogen ..	50	47
Chlorides	0.507	0.498

Normal rabbit starved to determine the effects of special diet and starvation.

Rabbit 29—Jejunal obstruction—3/5/28—Weight 7 pounds. Lettuce and bread diet 2 weeks: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	2 Hours After Release
Nonprotein nitrogen	40.8	141	156
Chlorides	0.496	0.380	0.389

Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
Stomach	153	0.256	0.395

Ethylene anesthesia 20 min. Obstruction, rubber band, third inch jejunum. Blood from ear. Stomach contents removed by catheter through esophagus 24 hours after obstruction. Obstruction released. Neither food nor water postoperatively until 2 hours after release. Rabbit died 29 hours after supposed release of obstruction. There was sufficient necrosis of the bowel wall from too much pressure to cause partial obstruction at point of constriction.

Rabbit 30—Jejunal obstruction—3/12/28. Weight 7½ pounds. Lettuce and bread diet 3 weeks:
No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	2 Hours After Release
Nonprotein nitrogen	30	103.8	86.3
Chlorides	0.481	0.409	0.418

Ethylene anesthesia 18 minutes. Obstruction, rubber band, third inch jejunum. Jejunum accidentally opened below point of obstruction and closed with silk purse-string. There was considerable free fluid in abdominal cavity at time of operation. Blood from ear. Obstruction released in 21 hours. Neither food nor water postoperatively until 2 hours after release of obstruction. Living and apparently healthy 1 week later.

Rabbit 31—Jejunal obstruction—3/12/28. Weight 4½ pounds. Lettuce and bread diet 3 weeks:
No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	2 Hours After Release
Nonprotein nitrogen.....	52.6	90	104.8
Chlorides	0.502	0.455	0.373

Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
Stomach	120	0.430	0.517

Ethylene anesthesia 15 minutes. Obstruction, rubber band, third inch jejunum. Stomach contents removed by catheter through esophagus 24 hours after obstruction. Obstruction released and 150 cc. of distilled water plus 0.4 Gm. NaCl given by catheter through esophagus. Neither food nor water postoperatively until 2 hours after release. Blood from ear. Rabbit died 48 hours after release from partial intestinal obstruction.

Rabbit 32—Jejunal obstruction—3/12/28. Weight 7½ pounds. Lettuce and bread diet 3 weeks:
No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	2 Hours After Release
Nonprotein nitrogen	61.2	102.5	87.8
Chlorides	0.502	0.413	0.426

Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
Stomach	157	0.449	0.705

Ethylene anesthesia 15 min. Obstruction, rubber band, third inch jejunum. Blood from ear. Stomach contents removed by catheter through esophagus in 24 hours. Obstruction released and 150 cc. of distilled water plus 0.5 cc. concentrated HCl, the chlorine content of which is equal to 0.4 Gm. NaCl, given by catheter through esophagus. Neither food nor water postoperatively until 2 hours after release. Living and apparently well 1 week later.

Rabbit 33—Jejunal obstruction—3/12/28. Weight 7¼ pounds. Lettuce and bread diet 3 weeks:
No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	2 Hours After Release	20 Hours After Release	44 Hours After Release
Nonprotein nitrogen	62.3	160	192	201	217
Chlorides	0.442	0.307	0.297	0.343	0.363

Ethylene anesthesia 15 minutes. Obstruction, rubber band, third inch jejunum. Blood from ear. Stomach contents removed by catheter through esophagus in 24 hours. Obstruction released. Neither food nor water allowed distilled water ad lib until 20 h. Obstruction. Slight consolidation of one lung. No other cause of death found.

Rabbit 34—Jejunal obstruction—3/26/28. Weight 5 pounds. Lettuce and bread diet 2 weeks:
No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	2 Hours After Release	20 Hours After Release	68 Hours After Release
Nonprotein nitrogen.....	51.5	126	134	250	63
Chlorides	0.479	0.435	0.403	0.419	0.495

Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
Stomach	101	0.107	0.108

Ethylene anesthesia 15 minutes. Obstruction, third inch jejunum, rubber band. Blood from ear. Stomach contents removed by catheter through esophagus in 24 hours. Obstruction released. Neither food nor water postoperatively until obstruction was released. Animal allowed distilled water ad lib until 20 hours after release, then food and water. Living and apparently healthy 1 week later.

Rabbit 25—Jejunal obstruction—3/26/28. Weight 5 pounds. Lettuce and bread diet 2 weeks:
No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	2 Hours After Release	20 Hours After Release	68 Hours After Release
Nonprotein nitrogen	60	129	144	183.5	27
Chlorides	0.462	0.440	0.435	0.452	0.452

Ethylene anesthesia 15 minutes. Obstruction, rubber band, third inch jejunum. Blood from ear. Attempt to remove stomach contents in 24 hours was unsuccessful. Obstruction released. Neither food nor water postoperatively until stomach was released. Distilled water ad lib until 20 hours after release, then food and water. It is possible that the obstruction in this animal was incomplete which would account for the peculiar figures and also for the unsuccessful attempt to remove stomach contents. Living and apparently healthy 1 week later.

Rabbit 40—Jejunal obstruction—4/9/28. Weight 6 pounds. Lettuce and bread diet 3 weeks:
No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	2 Hours After Release	18 Hours After Release	42 Hours After Release
Nonprotein nitrogen.....	51.2	152.6	126.5	156	84
Chlorides	0.528	0.347	0.422	0.336	0.561

Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
Stomach	158	0.395	0.625

Ethylene anesthesia 10 minutes. Obstruction, rubber band, third inch jejunum. Blood from ear. Stomach contents removed by catheter through esophagus in 24 hours. Impossible to empty stomach completely. Obstruction released and 150 cc. of distilled water plus 0.6 Gm. NaCl given by catheter through esophagus. Neither food nor water postoperatively until 2 hours after release, then distilled water ad lib until 18 hours after release, then food and water. Living and apparently healthy 1 week later.

Rabbit 41—Jejunal obstruction. 4/9/28. Weight 7 pounds. Lettuce and bread diet 3 weeks:
No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	2 Hours After Release	18 Hours After Release	42 Hours After Release
Nonprotein nitrogen	46	116.2	107	100	169
Chlorides	0.500	0.370	0.439	0.508	0.505

Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
Stomach	215	0.327	0.704

Ethylene anesthesia 10 minutes. Obstruction, rubber band, third inch jejunum. Blood from ear. Stomach contents removed by catheter through esophagus in 24 hours. There was considerable gas in the stomach. Obstruction released. 150 cc. distilled water containing HCl equivalent to 0.6 Gm. NaCl given by catheter through esophagus. Neither food nor water postoperatively until 2 hours after release, then distilled water ad lib until 18 hours after release, then food and water. Rabbit developed pneumonia and died 66 hours after release which probably accounts for the high N.P.N. noted at 42 hours after release.

Rabbit 42—Jejunal obstruction—4/9/28. Weight 5 pounds. Lettuce and bread diet 3 weeks:
No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	2 Hours After Release	18 Hours After Release	42 Hours After Release
Nonprotein nitrogen	45.8	168	105	100	57.5
Chlorides	0.500	0.307	0.424	0.424	0.508

Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
Stomach	160	0.328	0.526

Ethylene anesthesia 12 minutes. Obstruction, rubber band, third inch jejunum. Blood from ear. Stomach contents removed by catheter through esophagus in 24 hours. Obstruction released. 150 cc. distilled water plus 0.6 Gm. NaCl given by catheter through esophagus. Neither food nor water postoperatively until 2 hours after release, then distilled water ad lib until 18 hours after release, then food and water. Living and apparently healthy 1 week later.

Rabbit 61—Jejunal obstruction—5/15/28. Weight 5¼ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction
Nonprotein nitrogen ..	55.5	119.1
Chlorides	0.568	0.442
Alkali reserve	82.4

Ethylene anesthesia 6 minutes. Obstruction, umbilical tape, third inch jejunum. First blood from ear, second from heart. Bled from heart and killed in 24 hours. Last blood was somewhat clotted. Neither food nor water postoperatively.

Rabbit 62—Jejunal obstruction—5/15/28. Weight 6¾ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction
Nonprotein nitrogen ...	40.2	187
Chlorides	0.446	0.194
Alkali reserve	83.7

Ethylene anesthesia 6 minutes. Obstruction, umbilical tape, third inch jejunum. First blood from ear, second from heart. Bled and killed in 24 hours. Neither food nor water postoperatively.

Rabbit 70—Ileal obstruction—7/2/28. Weight 4½ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction
Nonprotein nitrogen ..	45.1	88.7
Chlorides	0.496	0.415
Alkali reserve	123

Ethylene anesthesia 6 minutes. Obstruction, umbilical tape, terminal ileum. First blood from ear, second from heart. Bled and killed in 24 hours. Almost no distention. Very hot day. Neither food nor water postoperatively.

Rabbit 71—Jejunal obstruction—7/2/28—Weight 4½ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction
Nonprotein nitrogen ...	41.3	152.6
Chlorides	0.488	0.420
Alkali reserve	69

Ethylene anesthesia 6 minutes. Obstruction, umbilical tape, third inch jejunum. First blood from ear, second from heart. Bled and killed in 24 hours. Slight distention. Very hot day. Neither food nor water postoperatively.

Rabbit 75—Jejunal obstruction—7/9/28. Weight 4½ pounds. Lettuce and bread diet 4 weeks: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours Obstruction	30 Hours Obstruction
Nonprotein nitrogen	53	142.8	172.4
Chlorides	0.441	0.404	0.379
Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
Stomach and duodenal.....	190	0.604	1.148

Ethylene anesthesia 6 minutes. Obstruction, umbilical tape, third inch jejunum. First two blood from ear, third from heart. Bled and killed in 30 hours. Stomach and duodenal contents removed. Rabbit very sick. Neither food nor water postoperatively.

Rabbit 78—Jejunal obstruction—7/23/28. Weight 4½ pounds. Lettuce and bread diet 2 weeks: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction		
Nonprotein nitrogen ..	38.9	142		
Chlorides	0.488	0.396		
Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.	
Stomach and duodenal.....	222	0.334	0.741	

Ethylene anesthesia 5 minutes. Obstruction, third inch jejunum, umbilical tape. First blood from ear, second from heart. Bled and killed in 24 hours. Stomach and duodenal contents removed. Rabbit not extremely sick. Neither food nor water postoperatively.

Rabbit No. 79—Ileal obstruction—7/23/28. Weight 4½ pounds. Lettuce and bread diet 2 weeks: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction		
Nonprotein nitrogen ..	65.2	104		
Chlorides	0.475	0.420		
Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.	
Stomach and intestinal.....	96	0.370	288	

Ethylene anesthesia 5 minutes. Obstruction, umbilical tape, terminal ileum. First blood from ear, second from heart. Bled and killed in 24 hours. Stomach and small intestinal contents removed. Rabbit not very sick. Neither food nor water postoperatively.

	Before Obstruction	26 Hours After Obstruction	2 Hours After Release	22 Hours After Release
Nonprotein nitrogen....	49.5	179.3	163.5	127.3
Chlorides	0.518	0.495	0.501	0.508

Rabbit 84—Jejunal obstruction—9/19/29. Lettuce and bread diet 4 weeks: No food for 48 hours.

Ethylene anesthesia 10 minutes. Obstruction, rubber band, third inch jejunum. Blood from ear. Stomach contents removed by catheter through esophagus in 24 hours. Obstruction released. 150 cc. distilled water plus 0.6 Gm. NaCl given by catheter through esophagus. Neither food nor water postoperatively until 22 hours after release of obstruction. Living and apparently healthy 1 week later.

PART II

Rabbit 12—Jejunostomy—3/29/27. General diet: No starvation.

	Before Operation	24 Hours After Operation
Nonprotein nitrogen ...	38	64.1
Chlorides	0.445	0.500

Ethylene anesthesia 20 minutes. Jejunostomy, third inch jejunum, by severing bowel, inserting rubber tube in proximal end and bringing it out through belly wall; distal end tied off and inverted by purse string. Blood from ear. Rabbit died in 36 hours. Jejunostomy functioned fairly well. Food and water allowed throughout procedure.

Rabbit 16—Jejunostomy—11/7/27. Weight $4\frac{1}{2}$ pounds. General diet: No food for 48 hours; water ad lib.

	Before Operation	25½ Hours After Operation		
Nonprotein nitrogen ...	43.1	188		
Chlorides	0.420	0.317		
Contents			Per Cent as NaCl	Total as NaCl, Gm.
Stomach and duodenal.....	39.5	(which equals no chlorides)	

Ethylene anesthesia 20 minutes. Jejunostomy, third inch jejunum, by severing bowel, inserting rubber tube in proximal end and bringing it out through belly wall; distal end tied off and inverted by purse string. Blood from ear. Rabbit killed in 25½ hours. Stomach and duodenal contents removed. Excellent functioning of jejunostomy. Rabbit fairly sick when killed. Neither food nor water postoperatively.

Rabbit 17—Jejunostomy—11/7/27. Weight $4\frac{1}{2}$ pounds. General diet: No food for 48 hours; water ad lib.

	Before Operation	25½ Hours After Operation		
Nonprotein nitrogen ...	52.1	198		
Chlorides	0.450	0.310		
Contents			Per Cent as NaCl	Total as NaCl, Gm.
Stomach and duodenal.....	49.5	(which equals no chlorides)	

Ethylene anesthesia 20 minutes. Jejunostomy, third inch jejunum, by severing bowel and suturing wall of proximal end to skin edge; distal end tied off and inverted by purse string. First blood from ear; second from heart. Rabbit killed in 25½ hours. Stomach and duodenal contents removed. Good functioning of jejunostomy. Rabbit fairly sick. Neither food nor water postoperatively.

Rabbit G3—Ileal obstruction—5/15/28. Weight 5 pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction
Nonprotein nitrogen ...	39.2	52.2
Chlorides	0.521	0.452
Alkali reserve	74.9

Ethylene anesthesia 8 minutes. Obstruction, umbilical tape, terminal ileum. Given 100 cc. water by catheter through esophagus immediately after obstruction. First blood from ear, second from heart. Bled and killed in 24 hours. Last blood slightly clotted. Almost no distention. Rabbit not obviously sick. Neither food nor water postoperatively.

Rabbit G4—Ileal obstruction—5/15/28. Weight $4\frac{3}{4}$ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction
Nonprotein nitrogen ...	48	77.7
Chlorides	0.515	0.363
Alkali reserve	83.7

Ethylene anesthesia 8 minutes. Obstruction, umbilical tape, terminal ileum. First blood from ear, second from heart. Given 100 cc. water by catheter through esophagus immediately after obstruction. Bled and killed in 24 hours. Rabbit not very sick. Neither food nor water postoperatively.

Rabbit 65—Jejunostomy—6/27/28. Weight $5\frac{1}{2}$ pounds. General diet: No food for 48 hours; water ad lib.

	Before Operation
Nonprotein nitrogen	30.5
Chlorides	0.498

Ethylene anesthesia 20 minutes. Jejunostomy, third inch jejunum, by severing bowel, inserting rubber tube in proximal end and bringing it out through belly wall; distal end tied off and inverted by purse string. Blood from ear. Rabbit died 16 hours after operation because of leak into peritoneal cavity. Allowed water postoperatively.

Rabbit 69—Ileal obstruction—7/2/28. Weight $4\frac{1}{2}$ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction
Nonprotein nitrogen ...	46.8	70
Chlorides	0.500	0.372
Alkali reserve	92

Ethylene anesthesia 6 minutes. Obstruction, umbilical tape, terminal ileum. First blood from ear, second from heart. Given 100 cc. water by catheter through esophagus immediately after obstruction and the same amount at 2, 4 and 6 hours after obstruction. Bled and killed in 24 hours. Not much distention. Very hot day. Rabbit not especially sick. Neither food nor water postoperatively.

Rabbit 72—Ileal obstruction—7/2/28. Weight $4\frac{1}{2}$ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction
Nonprotein nitrogen ...	57.1	74
Chlorides	0.524	0.417
Alkali reserve	83

Ethylene anesthesia 6 minutes. Obstruction, umbilical tape, terminal ileum. First blood from ear, second from heart. Given 100 cc. water by catheter through esophagus immediately after obstruction and the same amount 2, 4 and 6 hours after obstruction. Bled and killed in 24 hours. Little distention. Very hot day. Rabbit not especially sick. Neither food nor water postoperatively.

Rabbit 73—Jejunal obstruction—7/9/28. Weight $4\frac{1}{2}$ pounds. Lettuce and bread diet 4 weeks: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	30 Hours After Obstruction
Nonprotein nitrogen	51	103.9	222.2
Chlorides	0.425	0.400	0.396

Stomach Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
At 8 hours.....	66	0.490	0.323
At 16 hours.....	66	0.366	0.220
At 24 hours.....	45	0.544	0.245
At 30 hours.....	10	0.490	0.05

Ethylene anesthesia 6 minutes. Obstruction, umbilical tape, third inch jejunum. First two bloods from ear, third from heart. Stomach contents removed by catheter through esophagus at 8, 16 and 24 hours after obstruction. Bled, killed and stomach and duodenal contents removed 30 hours after obstruction. There was no distention of stomach and very little of duodenum. Rabbit had infected jaw. Neither food nor water postoperatively.

Rabbit 74—Jejunal obstruction—7/9/28. Weight $4\frac{1}{2}$ pounds. Lettuce and bread diet 4 weeks: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	30 Hours After Obstruction
Nonprotein nitrogen	36.2	109.2	154
Chlorides	0.439	0.401	0.396

Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
At 8 hours; stomach.....	65	0.498	0.324
At 16 hours; stomach.....	66	0.501	0.331
At 24 hours; stomach.....	43	0.465	0.200
At 30 hrs.; stomach and duodenal.	20	0.340	0.08

Ethylene anesthesia 6 minutes. Obstruction, umbilical tape, third inch jejunum. First two bloods from ear, third from heart. Stomach contents removed by catheter through esophagus at 8, 16 and 24 hours after obstruction. Bled, killed and stomach and duodenal contents removed 30 hours after obstruction. No distention of stomach; very slight distention of duodenum. Neither food nor water postoperatively.

Rabbit 76—Jejunal obstruction—7/9/28. Weight 4½ pounds. Lettuce and bread diet 4 weeks:
No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	30 Hours After Obstruction
Nonprotein nitrogen	39.9	129.8	157.3
Chlorides	0.427	0.391	0.349

Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
At 30 hrs.; stomach and duodenal..	286	0.356	1.018

Ethylene anesthesia 6 minutes. Obstruction, umbilical tape, third inch jejunum. First two bloods from ear, third from heart. Given 100 cc. water by catheter through esophagus at 8 hours and again at 16 hours after obstruction. Given 75 cc. water by catheter through esophagus at 24 hours after obstruction. Bled, killed and stomach and duodenal contents removed at 30 hours after obstruction. Rabbit very sick. Considerable distention. Neither food nor water postoperatively.

Rabbit 77—Jejunal obstruction—7/23/28. Weight 4 pounds. Lettuce and bread diet 2 weeks:
No food for 48 hours; water ad lib.

	Before Obstruction	19 Hours After Obstruction
Nonprotein nitrogen ...	58.8	200
Chlorides	0.502	0.346

Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
Stomach and duodenal.....	188	0.261	0.491

Ethylene anesthesia 5 minutes. Obstruction, umbilical tape, third inch jejunum. First blood from ear, second from heart. Given 100 cc. liquid alboline by catheter through esophagus immediately after obstruction and again 7 hours after obstruction. Dying, bled and killed 19 hours after obstruction. Stomach and duodenal contents removed. 200 cc. alboline discarded, the weight of stomach and duodenal contents being that left after removal of alboline. Neither food nor water postoperatively.

Rabbit 80—Ileal obstruction—7/23/28. Weight 4½ pounds. Lettuce and bread diet 2 weeks:
No food for 48 hours; water ad lib.

	Before Obstruction
Nonprotein nitrogen	43.3
Chlorides	0.492

Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
Stomach and intestinal.....	160	0.286	0.458

Ethylene anesthesia 5 minutes. Obstruction, umbilical tape, terminal ileum. Blood from ear. Given 100 cc. liquid alboline by catheter through esophagus immediately after obstruction and again 7 hours later. Given 75 cc. glycerin by catheter through esophagus 11 hours after obstruction. The glycerin was given by mistake instead of alboline. Rabbit died during night. Considerable hemorrhage into stomach. Stomach and duodenal contents removed a few hours after death. Neither food nor water postoperatively.

Rabbit 85—Jejunal obstruction—9/20/28. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	22 Hours After Obstruction
Nonprotein nitrogen ..	53.7	122
Chlorides	0.467	0.430

Ethylene anesthesia 6 minutes. Obstruction, umbilical tape, third inch jejunum. First blood from ear, second from heart. Given 120 cc. liquid alboline by catheter through esophagus immediately after obstruction. Bled and killed 22 hours after obstruction. Fairly sick. Neither food nor water postoperatively.

Rabbit 86—Jejunal obstruction—9/20/28. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	22 Hours After Obstruction
Nonprotein nitrogen ...	49.6	177
Chlorides	0.512	0.429

Ethylene anesthesia 6 minutes. Obstruction, umbilical tape, third inch jejunum. First blood from ear, second from heart. Given 120 cc. of stomach contents (obtained from rabbit 83 by catheter through esophagus 24 hours after jejunal obstruction) by catheter through esophagus immediately after obstruction. Stomach contents used within 1 hour after removal from rabbit 83. Bled and killed 22 hours after obstruction. Rabbit fairly sick. Neither food nor water postoperatively.

Rabbit 87—Jejunal obstruction—9/20/28. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	22 Hours After Obstruction
Nonprotein nitrogen ...	60	203
Chlorides	0.508	0.430

Ethylene anesthesia 6 minutes. Obstruction, umbilical tape, third inch jejunum. First blood from ear, second from heart. Given 120 cc. of stomach contents (obtained from rabbit 84 by catheter through esophagus 24 hours after jejunal obstruction) by catheter through esophagus immediately after obstruction. Stomach contents used within 1 hour after removal from rabbit 84. Bled and killed 22 hours after obstruction. Rabbit fairly sick. Neither food nor water postoperatively.

Rabbit 88—Ileal obstruction—9/25/28. Weight 5 pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction
Nonprotein nitrogen	366
Chlorides	0.492

Ethylene anesthesia 5 minutes. Obstruction, umbilical tape, terminal ileum. Blood from ear. Given 180 cc. liquid alboline by catheter through esophagus immediately after obstruction. Given 100 cc. liquid alboline by catheter through esophagus 8 hours after obstruction. Rabbit died during night; greatly distended, oil filling entire small intestine. Neither food nor water postoperatively.

Rabbit 89—Ileal obstruction—9/25/28. Weight 4½ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	22½ Hours After Obstruction
Nonprotein nitrogen ...	48.3	166.6
Chlorides	0.508	0.369

Ethylene anesthesia 5 minutes. Obstruction, umbilical tape, terminal ileum. First blood from ear, second from heart. Given 180 cc. liquid alboline by catheter through esophagus immediately after obstruction. Given 100 cc. liquid alboline by catheter through esophagus 8 hours after obstruction. Bled and killed 22½ hours after obstruction. Enormous distention. postoperatively.

Rabbit 90—Ileal obstruction—9/25/28. Weight 4½ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	22½ Hours After Obstruction
Nonprotein nitrogen ...	46.1	87.3
Chlorides	0.495	0.475

Ethylene anesthesia 5 minutes. Obstruction, umbilical tape, terminal ileum. First blood from ear, second from heart. Given 180 cc. stomach and duodenal contents (obtained from rabbit obstructed at third inch jejunum for 22 hr.) by catheter through esophagus immediately after obstruction. Given 100 cc. stomach and duodenal contents (obtained from rabbit obstructed at third inch jejunum for 26 hours) by catheter through esophagus 6 hours after obstruction. The stomach and duodenal contents were obtained from rabbits obstructed the previous day, killed at the end of 22 and 26 hours respectively, and their stomach and duodenal contents removed. The contents were used for ingestion into rabbit 90 within 1 hour after the death of the respective rabbit. Bled and killed 22½ hours after obstruction. Fairly sick but not nearly so much distention as was noted in 88, 89, 91. Neither food nor water postoperatively.

Rabbit 91—Ileal obstruction—9/25/28. Weight 4½ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	22½ Hours After Obstruction
Nonprotein nitrogen ...	50.1	157.7
Chlorides	0.512	0.438

Ethylene anesthesia 5 minutes. Obstruction, umbilical tape, terminal ileum. First blood from ear, second from heart. Given 180 cc. liquid alboline by catheter through esophagus immediately after obstruction. Given 100 cc. liquid alboline by catheter through esophagus 8 hours after obstruction. Bled and killed 22½ hours after obstruction. Rabbit very sick. Greatly distended. Neither food nor water postoperatively.

Rabbit 92—Jejunal obstruction—9/27/28. Weight 4½ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction
Nonprotein nitrogen ...	46.1	152.6
Chlorides	0.515	0.469

Ethylene anesthesia 15 minutes. Obstruction, umbilical tape, third inch jejunum. Gastrotomy by opening stomach through a wide incision and suturing mucous membrane to skin. Blood from ear. Died between 32 and 34 hours after operation. Stomach drained well so that there was no distention of stomach and very little of duodenum. Very little peritoneal reaction. Water ad lib postoperatively. No food.

Rabbit 94—Control operation—10/9/28. Weight 5 pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	46 Hours After Obstruction
Nonprotein nitrogen	40.5	58	48.7
Chlorides	0.462	0.462	0.479

Ethylene anesthesia 10 minutes. Anterior stomach wall sutured to anterior abdominal wall. Blood from ear. Water ad lib postoperatively; food after 46 hours. Rabbit living and apparently healthy 1 week later.

Rabbit 95—Pyloric obstruction—10/9/28. Weight 4½ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	28 Hours After Obstruction
Nonprotein nitrogen	46.1	202	232.5
Chlorides	0.446	0.317	0.330

Ethylene anesthesia 15 minutes. Obstruction, umbilical tape, pylorus. Gastrostomy by opening stomach through a wide incision and suturing mucous membrane to skin. There was considerable bleeding from incised stomach which was finally controlled by many sutures. First two bloods from ear, third from heart. Dying, bled and killed 28 hours after operation. There was a slight amount of hemorrhage around the pylorus and a small hematoma of the stomach wall. Very little peritoneal irritation. Water ad lib postoperatively. No food.

Rabbit 96—Pyloric obstruction—10/9/28. Weight 4½ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	44 Hours After Obstruction
Nonprotein nitrogen	50	103.6	243.9
Chlorides	0.420	0.366	0.257

Ethylene anesthesia 15 minutes. Obstruction, umbilical tape, pylorus. Gastrostomy by opening through a wide incision and suturing mucous membrane to skin. First two bloods from ear, third from heart. Dying, bled and killed 44 hours after operation. Very little peritoneal irritation. Water ad lib postoperatively. No food.

Rabbit 97—Control operation—10/9/28. Weight 4½ pounds. General diet: No food for 48 hours; water ad lib.

	Before Operation	24 Hours After Operation	46 Hours After Operation
Nonprotein nitrogen	40	60	54.9
Chlorides	0.478	0.470	0.479

Ethylene anesthesia 10 minutes. Anterior stomach wall sutured to anterior abdominal wall. Blood from ear. Water ad lib postoperatively. Food after 46 hours. Living and apparently healthy 1 week later.

Rabbit 102—Jejunal obstruction—11/1/28. Weight 4½ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction
Nonprotein nitrogen	56.8
Chlorides	0.462

Ethylene anesthesia 5 minutes. Obstruction, umbilical tape, third inch jejunum. Given 120 cc. 0.9 per cent NaCl by catheter through esophagus immediately after obstruction. Blood from ear. Died during night from ruptured duodenum. Neither food nor water postoperatively.

Rabbit 103—Ileal obstruction—11/1/28. Weight 4½ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	22½ Hours After Obstruction
Nonprotein nitrogen ...	46	116
Chlorides	0.475	0.424

Ethylene anesthesia 5 minutes. Obstruction, umbilical tape, terminal ileum. First blood from ear, second from heart. Given 180 cc. stomach and duodenal contents (obtained from rabbit with jejunal obstruction at 26 hours) by catheter through esophagus immediately after obstruction. Given 100 cc. stomach and duodenal contents (obtained from rabbit with jejunal obstruction at 26 hours) by catheter through esophagus 5 hours after obstruction. The stomach and duodenal contents were obtained from rabbits obstructed at third inch of jejunum the previous day and were used for rabbit 103 within 1 hour after the death of the rabbits. Bled and killed 22½ hours after obstruction. Neither food nor water postoperatively. Not very sick.

Rabbit 104—Jejunal obstruction—11/1/28. Weight $4\frac{1}{2}$ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction
Nonprotein nitrogen	55.2
Chlorides	0.492

Ethylene anesthesia 5 minutes. Obstruction, umbilical tape, third inch jejunum. Given 120 cc. stomach and duodenal contents (obtained from rabbit with jejunal obstruction for 26 hours) by catheter through esophagus immediately after obstruction. Stomach and duodenal contents used were obtained from rabbit obstructed the previous day and were used within 1 hour, after the death of the rabbit. Blood from ear. Died during night. Neither food nor water postoperatively.

Rabbit 105—Jejunal obstruction—11/1/28. Weight $4\frac{1}{2}$ pounds. General diet: No food for 48 hours; water ad lib.

	Before Obstruction	20 Hours After Obstruction
Nonprotein nitrogen ...	51	195
Chlorides	0.515	0.386

Ethylene anesthesia 5 minutes. Obstruction, umbilical tape, third inch jejunum. Given 120 cc. liquid alboline by catheter through esophagus immediately after obstruction. First blood from ear. Second from heart. Dying, bled and killed in 20 hours. Neither food nor water postoperatively.

PART III

Rabbit 36—Jejunal obstruction—4/2/28. Weight $4\frac{3}{4}$ pounds. Lettuce and bread diet for 3 weeks: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	Per Cent as NaCl	Total as NaCl, Gm.
Nonprotein nitrogen ...	40	104		
Chlorides	0.491	0.479		
Stomach Contents	Weight, Gm.			
At 8 hours.....	134.5		0.410	0.552
At 16 hours.....	149.0		0.225	0.336
At 24 hours.....	84.0		0.390	0.328
At 32 hours.....	64.0		0.267	0.171

Ethylene anesthesia 8 minutes. Obstruction, umbilical tape, third inch jejunum. Blood from ear. Stomach contents removed by catheter through esophagus at 8, 16, 24 and 32 hours after obstruction. 40 cc. 0.9 per cent NaCl given intravenously at 8, 16, 24 and 32 hours after obstruction. Rabbit died between 37 and 39 hours after obstruction. The duodenum was greatly distended, but the stomach was approximately normal in size and appearance. Neither food nor water postoperatively.

Rabbit 37—Jejunal obstruction—4/2/28. Weight $3\frac{1}{2}$ pounds. Lettuce and bread diet for 3 weeks: No food for 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	Per Cent as NaCl	Total as NaCl, Gm.
Nonprotein nitrogen ...	49.5	112.5		
Chlorides	0.473	0.528		
Stomach Contents	Weight, Gm.			
At 8 hours	128		0.343	0.439
At 16 hours	99		0.067	0.066

Ethylene anesthesia 8 minutes. Obstruction, umbilical tape, third inch jejunum. First blood from ear, second from heart. Stomach contents removed by catheter through esophagus at 8 and 16 hours after obstruction. Dying, bled and killed 24 hours after obstruction. Duodenum greatly distended. Stomach normal in size and appearance. Neither food nor water postoperatively.

Rabbit 38—Jejunal obstruction—4/2/28. Weight $4\frac{1}{2}$ pounds. Lettuce and bread diet 2 weeks: No food 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	29 Hours After Obstruction
Nonprotein nitrogen	35.8	85	111
Chlorides	0.531	0.554	0.620
Contents	Weight, Gm.	Per Cent as NaCl	Total as NaCl, Gm.
Stomach and duodenal.....	290	0.329	0.951

Ethylene anesthesia 8 minutes. Obstruction, umbilical tape, third inch jejunum. First two bloods from ear, third from heart. 40 cc. 0.9 per cent NaCl given intravenously at 8, 16 and 24 hours after obstruction. Bled and killed 29 hours after obstruction. Fairly sick. Stomach and duodenum greatly distended. Neither food nor water postoperatively.

Rabbit 39—Jejunal obstruction—4/2/28. Weight 4½ pounds. Lettuce and bread diet 2 weeks: No food 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	29 Hours After Obstruction
Nonprotein nitrogen	38.3	118.5	143
Chlorides	0.538	0.502	0.634
		Per Cent as NaCl	Total as NaCl, Gm.
Contents	Weight, Gm.		
Stomach and duodenal.....	390	0.353	1.377

Ethylene anesthesia 8 minutes. Obstruction, umbilical tape, third inch jejunum. First two bloods from ear, third from heart. 40 cc. NaCl given intravenously at 8, 16 and 24 hours after obstruction. Bled and killed 29 hours after obstruction. Fairly sick. Stomach and duodenum greatly distended. Neither food nor water postoperatively.

Rabbit 42—Jejunostomy—4/16/28. Lettuce and bread diet 10 days: No food 48 hours; water ad lib.

	Before Operation	24 Hours After Operation
Nonprotein nitrogen ...	53	96.6
Chlorides	0.496	0.545

Ethylene anesthesia 10 minutes. Jejunostomy, third inch jejunum, by bringing loop out through skin, completely severing it and tying off distal end. Blood from ear. 40 cc. 0.9 per cent NaCl given intravenously 8 and 16 hours after operation. Rabbit died 36 hours after operation. There was poor functioning of jejunostomy. Stomach and duodenum greatly distended. Neither food nor water postoperatively.

Rabbit 44—Jejunostomy—4/16/28. Lettuce and bread diet 10 days: No food 48 hours; water ad lib.

	Before Operation	24 Hours After Operation	37 Hours After Operation
Nonprotein nitrogen	58.8	148.8	274
Chlorides	0.512	0.429	0.375

Ethylene anesthesia 10 minutes. Jejunostomy, third inch jejunum, by bringing loop out through skin, completely severing it and tying off distal end. First two bloods from ear, third from heart. 40 cc. 5 per cent dextrose given intravenously 8 and 16 hours after operation. Bled and killed 37 hours after operation. Fairly sick. Fair functioning of jejunostomy although there was some distention of stomach and duodenum. Neither food nor water postoperatively.

Rabbit 45—Jejunostomy—4/16/28. Lettuce and bread diet 10 days: No food 48 hours; water ad lib.

	Before Operation	24 Hours After Operation	37 Hours After Operation
Nonprotein nitrogen	60	151.5	251
Chlorides	0.462	0.440	0.380

Ethylene anesthesia 10 minutes. Jejunostomy, third inch jejunum, by bringing out loop through skin, completely severing it and tying off distal end. First two bloods from ear, third from heart. 40 cc. 5 per cent dextrose given intravenously 8 and 16 hours after operation. Bled and killed 37 hours after operation. Fairly sick. Poor functioning of jejunostomy since duodenum was distended. Neither food nor water postoperatively.

Rabbit 46—Jejunal obstruction—4/23/28. Weight 4½ pounds. General diet: No food 48 hours; water ad lib.

	Before Obstruction	26 Hours After Obstruction		
Nonprotein nitrogen ...	38	125.5		
Chlorides	0.475	0.353		
			Per Cent as NaCl	Total as NaCl, Gm.
Contents	Weight, Gm.			
Stomach and duodenal.....	278	0.318		0.884

Ethylene anesthesia 6 minutes. Obstruction, umbilical tape, third inch jejunum. First blood from ear, second from heart. 40 cc. 0.9 per cent dextrose given intravenously 8 and 16 hours after obstruction. Bled and killed in 26 hours. Fairly sick. Stomach and duodenal contents removed. Neither food nor water postoperatively.

Rabbit 47—Jejunal Obstruction—4/23/28. Weight 3¾ pounds. General diet: No food 48 hours; water ad lib.

	Before Obstruction	26 Hours After Obstruction		
Nonprotein nitrogen ...	53	124.5		
Chlorides	0.473	0.538		
			Per Cent as NaCl	Total as NaCl, Gm.
Contents	Weight, Gm.			
Stomach and duodenal.....	251	0.431		1.082

Ethylene anesthesia 6 minutes. Obstruction, umbilical tape, third inch jejunum. First blood from ear, second from heart. 40 cc. 0.9 per cent NaCl given intravenously 8 and 16 hours after obstruction. Bled and killed in 26 hours. Fairly sick. Stomach and duodenal contents removed. Neither food nor water postoperatively.

Rabbit 48—Jejunal obstruction—4/23/28. Weight $3\frac{1}{2}$ pounds. General diet: No food 48 hours; water ad lib.

	Before Obstruction	26 Hours After Obstruction	Per Cent as NaCl	Total as NaCl, Gm.
Nonprotein nitrogen ...	51	139.5		
Chlorides	0.472	0.340		
Contents				
Stomach and duodenal.....	217		0.359	0.816

Ethylene anesthesia 6 minutes. Obstruction, umbilical tape, third inch jejunum. First blood from ear, second from heart. 40 cc. 5 per cent dextrose given intravenously 8 and 16 hours after obstruction. Bled and killed in 26 hours. Fairly sick. Stomach and duodenal contents removed. Neither food nor water postoperatively.

Rabbit 49—Jejunal obstruction—4/23/28. Weight $3\frac{1}{4}$ pounds. General diet: No food 48 hours; water ad lib.

	Before Obstruction	26 Hours After Obstruction	Per Cent as NaCl	Total as NaCl, Gm.
Nonprotein nitrogen ...	56	140.8		
Chlorides	0.515	0.545		
Contents				
Stomach and duodenal.....	246		0.388	0.955

Ethylene anesthesia 6 minutes. Obstruction, umbilical tape, third inch jejunum. First blood from ear, second from heart. 40 cc. 0.9 per cent NaCl given intravenously 8 and 16 hours after obstruction. Bled and killed in 26 hours. Fairly sick. Stomach and duodenal contents removed. Neither food nor water postoperatively.

Rabbit 50—Control—4/27/28. Weight $2\frac{1}{2}$ pounds. General diet: No starvation.

	Before	24 Hours After
Nonprotein nitrogen ...	33.5	62.8
Chlorides	0.462	0.412
Alkali reserve	95

First blood from ear, second from heart. 20 cc. 3 per cent sodium bicarbonate given intravenously at the beginning and again in 12 hours. Bled and killed 24 hours after first injection. No food after first injection. Distilled water ad lib.

Rabbit 51—Control—4/27/28. Weight $2\frac{1}{2}$ pounds. General diet: No starvation.

	Before	24 Hours After
Nonprotein nitrogen ...	30.5	56.5
Chlorides	0.459	0.402
Alkali reserve	86.2

First blood from ear, second from heart. 20 cc. 3 per cent sodium bicarbonate given intravenously at the beginning and again in 12 hours. Bled and killed 24 hours after first injection. No food after first injection. Distilled water ad lib.

Rabbit 52—Control—5/4/28. Weight $5\frac{1}{2}$ pounds. General diet: No food 48 hours; water ad lib.

	Before	24 Hours After
Nonprotein nitrogen ...	37	41
Chlorides	0.492	0.517
Alkali reserve	61.4

First blood from ear, second from heart. 30 cc. $2\frac{1}{2}$ per cent dextrose given intravenously at the beginning and again in 10 hours. Bled and killed 24 hours after first injection. No food after first injection. Distilled water ad lib.

Rabbit 53—Control—5/4/28. Weight $4\frac{3}{4}$ pounds. General diet: No food 48 hours; water ad lib.

	Before	24 Hours After
Nonprotein nitrogen ...	32	42
Chlorides	0.479	0.462
Alkali reserve	65.4

First blood from ear, second from heart. 30 cc. 3 per cent sodium bicarbonate neutralized with lactic acid given intravenously at the beginning and again in 10 hours. Bled and killed 24 hours after first injection. No food after first injection. Distilled water ad lib.

Rabbit 54—Control—5/4/28. Weight $5\frac{1}{2}$ pounds. General diet: No food 48 hours; water ad lib.

	Before	24 Hours After
Nonprotein nitrogen ...	35.7	46.5
Chlorides	0.492	0.465
Alkali reserve	54

First blood from ear, second from heart. 20 cc. 1 per cent lactic acid given intravenously at beginning and again in 10 hours. Bled and killed 24 hours after first injection. No food after first injection. Distilled water ad lib. Attempts to give 3 per cent lactic acid intravenously killed 3 rabbits immediately.

Rabbit 55—Control—5/4/28. Weight 5 pounds. General diet: No food 48 hours; water ad lib.

	Before	24 Hours After
Nonprotein nitrogen ...	37.2	61.2
Chlorides	0.498	0.469
Alkali reserve	81.5

First blood from ear, second from heart. 30 cc. 3 per cent sodium bicarbonate given intravenously at the beginning and again in 10 hours. Bled and killed 24 hours after first injection. No food after first injection. Distilled water ad lib.

Rabbit 56—Control—5/15/28. Weight 5 pounds. General diet: No food 24 hours; water ad lib. Alkali reserve.....56.4. Blood from heart; rabbit killed.

Rabbit 57—Jejunal obstruction—5/7/28. Weight 5½ pounds. General diet: No food 48 hours; water ad lib.

	Before Obstruction
Nonprotein nitrogen	29.3
Chlorides	0.479

Ethylene anesthesia 7 minutes. Obstruction, umbilical tape, third inch jejunum. Blood from ear. 40 cc. 0.9 per cent NaCl given intravenously 8 and 16 hours after obstruction. Died about 18 hours after obstruction. Stomach and duodenum enormously distended. Neither food nor water postoperatively.

Rabbit 58—Jejunal obstruction—5/7/28. Weight 5½ pounds. General diet: No food 48 hours; water ad lib.

	Before Obstruction	20 Hours After Obstruction
Nonprotein nitrogen ...	42.5	152.6
Chlorides	0.528	0.380
Alkali Reserve	65.5

Ethylene anesthesia 7 minutes. Obstruction, umbilical tape, third inch jejunum. First blood from ear, second from heart. 40 cc. 5 per cent dextrose given intravenously 8 and 16 hours after obstruction. Bled and killed 20 hours after obstruction. Not very sick. Neither food nor water postoperatively.

Rabbit 59—Jejunal obstruction—5/7/28. Weight 6 pounds. General diet: No food 48 hours; water ad lib.

	Before Obstruction	20 Hours After Obstruction
Nonprotein nitrogen ...	48.7	132.4
Chlorides	0.503	0.538
Alkali reserve	58

Ethylene anesthesia 7 minutes. Obstruction, umbilical tape, third inch jejunum. First blood from ear, second from heart. 40 cc. 0.9 per cent NaCl given intravenously 8 and 16 hours after obstruction. Bled and killed 20 hours after obstruction. Not very sick. Neither food nor water postoperatively.

Rabbit 60—Jejunal obstruction—5/7/28. Weight 5¼ pounds. General diet: No food 48 hours; water ad lib.

	Before Obstruction	20 Hours After Obstruction
Nonprotein nitrogen ...	26.3	103.6
Chlorides	0.515	0.373
Alkali reserve	63.5

Ethylene anesthesia 7 minutes. Obstruction, umbilical tape, third inch jejunum. First blood from ear, second from heart. 40 cc. 5 per cent dextrose given intravenously 8 and 16 hours after obstruction. Bled and killed 20 hours after obstruction. Not very sick. Neither food nor water postoperatively.

Rabbit 66—Jejunostomy—6/27/28—Weight 4½ pounds. General diet: No food 48 hours; water ad lib.

	Before Obstruction	26 Hours After Obstruction
Nonprotein nitrogen ...	75.9	80.6
Chlorides	0.465	0.501

Ethylene anesthesia 15 minutes. Jejunostomy, third inch jejunum, by severing jejunum, placing small rubber tube in proximal end and bringing it out through belly wall. Distal end tied off and inverted by purse string. First blood from ear, second from heart. 40 cc. 0.9 per cent NaCl given intravenously 8 and 16 hours after operation. Bled and killed in 26 hours. Very sick. Very slight peritoneal irritation. Stomach almost empty and but little dilation of duodenum. Neither food nor water postoperatively.

Rabbit 67—Jejunostomy—6/27/28. Weight 5 pounds. General diet: No food 48 hours; water ad lib.

	Before Operation	26 Hours After Operation
Nonprotein nitrogen ...	39.8	107
Chlorides	0.498	0.460

Ethylene anesthesia 15 minutes. Jejunostomy, third inch jejunum, by severing jejunum, placing rubber tube in proximal end and bringing it out through belly wall. Distal end tied off and inverted by purse string. First blood from ear, second from heart. 40 cc. 5 per cent dextrose given intravenously 8 and 16 hours after operation. Bled and killed 26 hours after operation. Quite sick. Slight peritoneal irritation. Stomach fairly well emptied. Duodenum slightly distended. Neither food nor water postoperatively.

Rabbit 68—Jejunostomy—6/27/28. Weight 4½ pounds. General diet: No food 48 hours; water ad lib.

	Before Operation	26 Hours After Operation
Nonprotein nitrogen ...	50	113
Chlorides	0.498	0.564

Ethylene anesthesia 15 minutes. Jejunostomy, third inch jejunum, by severing jejunum, placing rubber tube in proximal end and bringing it out through belly wall. Distal end tied off and inverted by purse string. First blood from ear, second from heart. 40 cc. 0.9 per cent NaCl given intravenously 8 and 16 hours after operation. Very sick. Bled and killed in 26 hours. Slight peritoneal irritation. Stomach nearly empty. Duodenum slightly distended. Neither food nor water postoperatively.

Rabbit 82—Jejunostomy—9/17/28. General diet: No food 48 hours; water ad lib.

	Before Operation	24 Hours After Operation	47 Hours After Operation
Nonprotein nitrogen	58.8	112.3	224.3
Chlorides	0.508	0.578	0.548

On 7/16/28 preliminary operation was done bringing loop of jejunum up through abdominal wall and suturing it in position, leaving only skin covering intestine; ½ per cent procaine hydrochloride anesthesia. Skin opened. Jejunum severed, distal end tied off. First two bloods from ear, third from heart. 40 cc. 0.9 per cent NaCl given intravenously 8, 16, 24, 32 and 40 hours after operation. Dying, bled and killed in 47 hours. Stomach empty. Very slight dilation of duodenum. Neither food nor water postoperatively.

Rabbit 93—Jejunal obstruction—9/27/28. Weight 4½ pounds. General diet: No food 48 hours; water ad lib.

	Before Obstruction	24 Hours After Obstruction	36 Hours After Obstruction
Nonprotein nitrogen	44	157.4	208.3
Chlorides	0.459	0.452	0.376

Ethylene anesthesia 15 minutes. Obstruction, umbilical tape, third inch jejunum. Gastrostomy by opening stomach through a wide incision and suturing mucous membrane to skin. First two bloods from ear, third from heart. 40 cc. 2½ per cent dextrose given subcutaneously 8, 16, 24 and 32 hours after obstruction. Dying, bled and killed in 36 hours. Very little peritoneal irritation. Stomach empty. Duodenum moderately distended. Neither food nor water postoperatively.

Rabbit 98—Pyloric obstruction—10/17/28. Weight 4 pounds. General diet: No food 48 hours; water ad lib.

	Before Obstruction	23 Hours After Obstruction
Nonprotein nitrogen ...	46.8	240.9
Chlorides	0.462	0.307

Ethylene anesthesia 15 minutes. Obstruction, umbilical tape, pylorus. Gastrostomy by opening stomach through a wide incision and suturing mucous membrane to skin. First blood from ear, second from heart. 40 cc. 2½ per cent dextrose given intravenously 7, 13 and 23 hours after obstruction. Dying, bled and killed in 23 hours. Very slight peritoneal irritation. Stomach empty. No food. Water ad lib.

Rabbit 99—Pyloric obstruction—10/17/28. Weight 4 pounds. General diet: No food 48 hours; water ad lib.

	Before Obstruction
Nonprotein nitrogen	44.7
Chlorides	0.495

Ethylene anesthesia 15 minutes. Obstruction, umbilical tape, pylorus. Gastrostomy by opening stomach through a wide incision and suturing mucous membrane to skin. Blood from ear. Considerable bleeding from stomach wall controlled by many sutures. 40 cc. 0.9 per cent NaCl given intravenously 7 and 13 hours after obstruction. Died during night. No food. Water ad lib.

Rabbit 100—Pyloric obstruction—10/17/28. Weight 4 pounds. General diet: No food 48 hours; water ad lib.

Before Obstruction

Nonprotein nitrogen	39.7
Chlorides	0.476

Ethylene anesthesia 15 minutes. Obstruction, umbilical tape, pylorus. Gastrostomy by opening stomach through a wide incision and suturing mucous membrane to skin. Moderate bleeding from stomach. Blood from ear. 40 cc. 2½ per cent dextrose given intravenously 7 and 13 hours after obstruction. Died during night. No food. Water ad lib.

Rabbit 101—Pyloric obstruction—10/17/28. Weight 4 pounds. General diet: No food 48 hours; water ad lib.

	Before Obstruction	48 Hours After Obstruction	67 Hours After Obstruction
Nonprotein nitrogen	45.4	145.9	220.8
Chlorides	0.488	0.393	0.343

Ethylene anesthesia 15 minutes. Obstruction, umbilical tape, pylorus. Gastrostomy by opening stomach through wide incision and suturing mucous membrane to skin. First two bloods from ear, third from heart. 40 cc. 0.9 per cent NaCl given intravenously 7 and 13 hours after operation and subcutaneously 30, 35, 46, 52 and 58 hours after operation. Unable to bleed at 24 hours. Bled with difficulty at 48 hours. Dying, bled and killed at 67 hours. Stomach empty. Very slight peritoneal irritation. No food. Water ad lib.

A COMPARATIVE STUDY OF THE BACTERICIDAL VALUES OF TWENTY-ONE COMMONLY USED ANTISEPTICS *

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This paper is the third in a series of studies of antiseptics. The first was a study of the bactericidal effect of mercurochrome-220 soluble¹ on *Bacillus pyocyaneus*, while the second² was an investigation of some of the properties of the antiseptic known as S. T. 37, described in 1927 by Leonard and Feirer.³ The present article is the direct outgrowth of the first two papers, and has for its object a comparative study, in vitro, of the bactericidal effect of twenty-one commonly used antiseptics on four different organisms growing on agar slants.

The organisms used were a freshly isolated strain of *Staphylococcus aureus*, a similar strain of *Bacillus pyocyaneus*, and laboratory stock cultures of *Bacillus subtilis* and *Bacillus typhosus*. Preliminary to the actual experimental work, each culture was transplanted for five successive days on agar slants. Immediately preceding experimentation, two fresh transplants were made from the fifth daily culture to agar slants. These were labeled B and X, while the parent culture was labeled A. Culture X served as a control of growth; A was a twenty-four hour old culture; while B was a freshly inoculated slant. Twenty-one such groups were made up using each of the four organisms employed (fig. 1).

To each of the twenty-one A and B groups of the four cultures, a different antiseptic was added in such quantity that when the culture tube was held in the vertical position, the slant surface was entirely covered by the antiseptic solution, insuring continuous contact of the agar slant surface with its culture and the antiseptic. At intervals of 15, 30, 60 and 180 minutes, transplants were made from the A and B tubes to fresh agar slants A', A'', B', B'', etc. A previously flamed

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¹ From the Department of Laboratories of the New York Post Graduate Medical School and Hospital.

1. Wright, I. S.: Effect of Mercurochrome-220 Soluble on the Growth of *Bacillus Pyocyaneus*, Arch. Surg. **15**:958 (Dec) 1928.

2. Allen, A. W., and Wright, I. S.: The Bactericidal Properties of the Solution S. T. 37, Arch. Surg. **17**:834 (Nov.) 1928

3. Leonard, Veader; and Feirer, W. A.: Bactericidal Activity of Hexylresorcinol in Glycerine, Bull. Johns Hopkins Hosp. **41**:21 (May) 1927; Hexylresorcinol as a General Antiseptic, Surg. Gynec. Obst **45**:603 (Nov.) 1927.

platinum loop was inserted into the supernatant antiseptic fluid, down to the agar surface, where the loop was drawn across the agar slant surface with its bacterial covering. This loopful of suspension was withdrawn through the antiseptic fluid above and streaked on a fresh agar slant. These tubes plus the originals were incubated at 37 C. for twenty-four hours and then observed. The entire experiment was repeated as a check on the first series.

The antiseptics used were obtained from the hospital pharmacy and conformed to the requirements as indicated in table 1. Dakin's solution was prepared according to the directions of Carrel,⁴ and used the same day. Both Dakin's solution and Zonite were titrated by the method of the same author. The agar was the usual meat infusion agar titrated to a p_H of 7.4.

Of the antiseptics listed, some are used routinely preoperatively, or as prophylactics against infection; others are applied to grossly

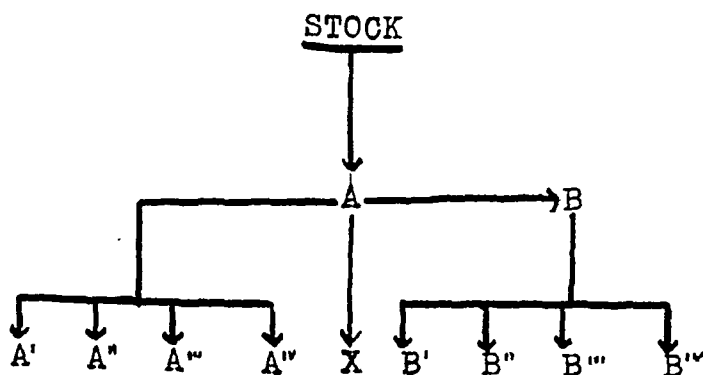


Fig. 1.—A diagram showing the origin of the cultures.

infected wounds; those of a third group are employed as antiseptic or germicidal irrigants. In this discussion, no such classification is made. Instead, they are arbitrarily grouped as dyes, halogens, heavy metals, miscellaneous, oxidizers and phenols, according to their exact or most apparent composition (table 2). Obviously, such a classification is approximate at best, and open to criticism. However, this classification with its shortcomings serves the purpose of this paper. It may be remarked in passing that the miscellaneous group should perhaps be called the alcoholic group, since all but one contain a large percentage of alcohol in addition to the other substances present.

This method of determining the bactericidal values of antiseptics is open to criticism. It may be said that it is not a standard method of determining the bactericidal properties of antiseptics. In practice, one

4. Carrel, A.: Communication to the Editor, J. A. M. A. 67:1777 (Dec.) 1916.

does not routinely or continuously immerse the contaminated or infected field in any antiseptic. Still less is one able to suspend the organisms in the antiseptic as represented by the Rideal-Walker⁵ or the Hygienic Laboratory procedure.⁶

In this work, attention is called to the fact that the penetrating power of each antiseptic was allowed to exert whatever influence it

TABLE 1.—*The Antiseptics Used in the Study, with Notes*

Dichloramine T, 5 per cent N.N.R.
Harrington's solution (Harrington, Charles: Some Studies in Asepsis, Ann. Surg. 40:475 (Oct.) 1904)
Silver nitrate, 10 per cent, prepared and used the same day
Zonite, original bottle, full strength, titer 1.10 per cent NaClO
Cresol compound, 2 per cent, U.S.P. (Iysol)
Potassium mercuric iodide of the salt, Gm. 4, acetone 400 cc.
Dakin's solution, N.N.R., prepared and used the same day, titer 0.5 per cent NaCl
Tincture of green soap, U.S.P.
Solution of iodine (Lugol's solution) 5 per cent, U.S.P.
Tincture of iodine, 7 per cent, U.S.P.
Protargin mite (argyrol) 20 per cent, N.N.R., prepared and used the same day
Alcohol, ethyl, 80 per cent
Hydrogen peroxide, solution, U.S.P., original recently received bottle
S. T. 37 (solution hexylresorcinols 1:1,000), original bottle
Mercuric chloride solution, 1:1,000
Mercurochrome-220 soluble, 2 per cent aqueous solution, N.N.R.
Listerine, original bottle, full strength
Phenol, 1:1,000
Acridlavine, neutral, 1:1,000, N.N.R., prepared and used the same day
Potassium permanganate, 1:1,000, prepared and used the same day
Boric acid, saturated solution at room temperature

TABLE 2.—*The Classification of the Antiseptics Employed, with the Number of Sterile Transplants for Each Antiseptic*

Halogens		Miscellaneous	
Dichloramine T, 5 per cent.....	64	Harrington's solution.....	64
Zonite.....	61	Potassium mercuric iodide.....	50
Dakin's solution.....	49	Tincture of green soap.....	49
Solution of iodine, 5 per cent.....	48	Alcohol, ethyl, 80 per cent.....	42
Tincture of iodine, 7 per cent.....	48	Listerine.....	13
Heavy Metals		Phenols	
Silver nitrate, 10 per cent.....	64	Cresol compound (Iysol) 2 per cent.....	51
Protargin mite (argyrol).....	43	S. T. 37, sol. hexylresorcinol, 1:1,000.....	21
Mercuric chloride, 1:1,000.....	18	Phenol, 1:1,000.....	10
Boric acid.....	3		
Oxidizers		Dyes	
Hydrogen peroxide.....	38	Mercurochrome, 2 per cent.....	16
Potassium permanganate.....	7	Acridlavine, neutral, 1:1,000.....	8

possessed on the bacteria; that incident to transplanting the bacteria there was a certain degree of agitation of the bacteria causing a certain amount of suspension of the organisms in the antiseptic solution for a shorter period of time than that named; and that, in addition, a certain

5. Rideal, S., and Walker, J. T. A.: Standardization of Disinfectants, J. Roy. San. Inst. 24:424, 1903.

6. Anderson, J. F., and McClintock, T. B.: A Method for the Bacteriological Standardization of Antiseptics, J. Infect. Dis. 8:1, 1911. Harrington, Charles: Some Studies in Asepsis, Ann. Surg. 40:475 (Oct.) 1904.

amount of the antiseptic was of necessity carried over to the fresh agar slants along with each inoculum of the A', B', etc., tubes.

In practice, one deals with two situations; the one a massive infection characterized usually by pus; the other, mere contamination. The present schema was devised to compare simultaneously, and under as nearly exact conditions as possible, the germicidal effect of the twenty-one antiseptics, under stated conditions, (1) on the type of organism used in determining the phenol coefficient; (2) on three different organ-

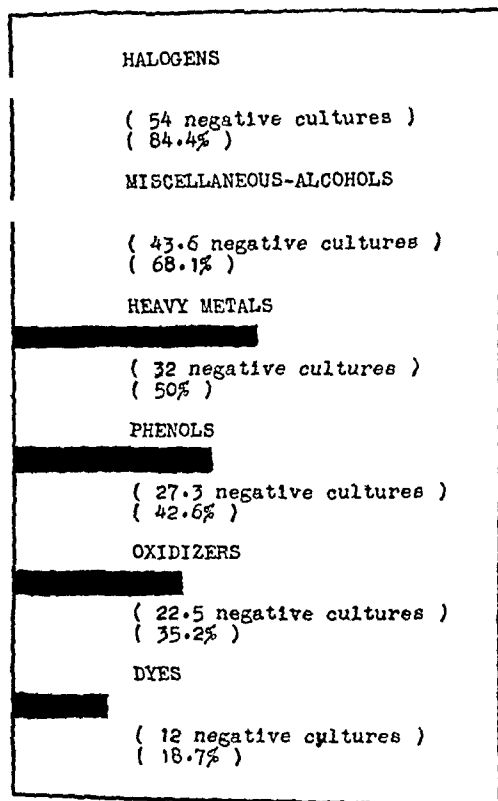


Fig. 2.—A diagram showing the relative efficiency of each of the six types of antiseptics used.

isms, roughly typical of three different classes of invaders; (3) under a condition simulating that most frequently met in routine practice: namely, surface and subsurface massive contamination.

Bacillus typhosus was employed because it is the organism used at present in determining the phenol coefficient of antiseptics. *Staphylococcus aureus* is a common contaminating and infecting organism relatively resistant to antiseptics in vivo, and is roughly characteristic of the pyogenic group. *Bacillus pyocyaneus* is a relatively frequent secondary invader. It is generally more resistant to antiseptics than

TABLE 3.—*The Aniseptics Used, Ranked in Order of Bactericidal Power*

[illegible]

* + Indicates growth of transplant; —, no growth of transplant.

Staphylococcus aureus. It is somewhat typical of the gram-negative bacilli. *Bacillus subtilis*, while not a pathogen, is a spore former, and was used because of that characteristic.

Omitting the control cultures, there were sixty-four transplants of each organism-antiseptic group. Since the negative cultures are indicative of germicidal value, the antiseptics have been listed in descending order of the number of sterile subcultures (table 3). In computing the results for figure 2, the negative cultures of each antiseptic of the six major subdivisions have been totaled and divided by the component number of the group. The percentages expressed are on the basis of sixty-four. From this computation, and also table 3, it is evident that the comparative rating of the antiseptic groups is as follows: halogens, miscellaneous, heavy metals, phenols, oxidizers and dyes.

COMMENT

The value of an antiseptic is commonly expressed in terms of its phenol coefficient. Especially is this true commercially. The bacterium employed in the determination of the phenol coefficient is the *Bacillus typhosus*. Although this procedure is of definite theoretic value, from a practical point of view, it has certain disadvantages. It is known that the organism of typhoid fever has relatively little resistance against many of the commonly used antiseptics. This is well illustrated by the results shown in table 3. If one contrasts the number of positive transplants of the typhoid group with the number of similar subcultures of any other group, it is obvious that the phenol coefficient is at best but superficially relevant to the actual practical bactericidal value of any antiseptic. It is a remote approximation.

CONCLUSIONS

1. The bactericidal efficacy of each of twenty-one commonly used antiseptics was tested against four different organisms.
2. The halogen group, as determined by this study, is the most efficacious of the antiseptic groups.
3. The phenol coefficient value stated as an index of practical bactericidal efficacy is unsatisfactory. The present methods of judging antiseptics do not constitute an accurate index of their practical worth.
4. The need for a comparative study of the bactericidal value of an antiseptic under a variety of conditions before it is offered to the public will be discussed in a later communication.

SURGICAL DISEASES OF THE COLON

COOPERATIVE MANAGEMENT *

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The strikingly successful end-results following cooperative management of cases of toxic goiter, of complicated cases of peptic ulcer and of other types of diseases requiring specialized preoperative and postoperative attention find a decidedly suggestive parallel in the group management of surgical diseases of the colon. The combination of resources made available by isolation of patients with surgical lesions of the colon into a single division under the combined management of surgeon and clinician has brought results as striking, in our experience, in the short length of time in which it has been employed, as the results obtained from any segregated group of unusual cases. Not only has isolation of these patients afforded individualization, with better selection of cases for different types of operation, but collective management in the postoperative period has been equally invaluable. Colonic conditions are complicated; they extend over a long period before the patients who suffer from them submit to surgical procedures, and therefore colonic cases have borne not only an unjustifiable surgical mortality but an undeserved reputation for high morbidity and unfavorable prognosis. The grouping of patients with surgical conditions of the colon in a division apart from that of general surgery, and the insistence that their preoperative management be cooperative and directed along distinct lines and that the surgical management at operation be carried out by a small group of surgeons particularly interested in these diseases have, we believe, materially aided us from every standpoint.

During the six months beginning Oct. 1, 1927, and ending April 1, 1928, 147 patients with colonic disease for whom surgical treatment has been prescribed have been isolated in a single section under the medical supervision of A. H. Logan and J. Arnold Borgen, and have been operated on by Walter E. Sistrunk and Fred W. Rankin. Multiple operations were done in practically every instance in this group of cases. In 103 cases two or more operations were performed, and in seven cases as many as four operations. The cases are divided as follows:

* Submitted for publication, Nov. 26, 1928.

* From the Divisions of Surgery and Medicine, The Mayo Clinic.

ninety-four of carcinoma of the rectum, rectosigmoid and sigmoid, five of carcinoma of the descending colon, three of carcinoma of the splenic flexure, five of carcinoma of the transverse colon, one large polyp of the transverse colon, four of carcinoma of the hepatic flexure, six of carcinoma of the cecum, one of carcinoma of the jejunum, three of diverticulitis of the sigmoid with abscess, ten of inflammatory cecal and pericecal lesions, seven of repair of postoperative fistula of the colon, four of resection for rectal stricture, two of closure of colostomy opening made elsewhere, one of resection of a portion of the ileum for obstruction with chronic ulcerative colitis and one of ileosigmoidostomy for a suspected malignant condition following healing chronic ulcerative colitis.

Of the 147 patients operated on, fourteen died, a total mortality of 9.6 per cent. There was only one death from preliminary colostomy in 108 operations; this occurred in a case of inoperable carcinoma of the rectum with obstruction. In the ninety-four cases of carcinoma of the rectum, rectosigmoid and sigmoid there were six deaths following resection, a mortality of 6.47 per cent. Of the fourteen deaths, eight occurred in cases which were pronounced inoperable at the time of exploration.

The preliminary preparation, the change in type of anesthesia and the coordinated postoperative management have resulted in lowering the number of postoperative complications, in the diminution in the number of fatal operative cases and in the application of more radical surgical procedures to the group. One of the most important factors in the treatment in colonic cases is preoperative preparation of the patient by the introduction of rehabilitation measures in addition to the application of local medicaments to the bowel to reduce the virulence of the organisms present and to overcome any obstruction which may have taken place. During the period of preoperative preparation, thorough cleansing of the bowel and filling the patient with foods which have a minimum of residue and may be stored for reserve is essential. The diet consists of a basic allowance of 2,000 calories of carbohydrate, including principally candy and fruit juices. To this, if the patients tolerate it, and the majority do, is added 50 per cent more carbohydrate, making a total of 3,000 calories daily. At ordinary rest, a patient will gain weight on such a diet; yet the bowel will remain comparatively empty. A daily urinalysis is made to note any overflow of the sugar threshold, and the results are checked by a determination of blood sugar which is made at the time of admission and again after a few days on the diet. Sugar rarely will appear in the urine, although there is usually an elevation of the blood sugar within normal limits. Many of these patients are in the later years of life, when tolerance for carbohydrate is more or less reduced; for these patients we have the basic

diet of 2,000 calories of carbohydrate to which is added a variable amount of protein or fat of low residue, or a combination of both. For convenience in calculation we add 25 per cent of fat or 25 per cent of protein, or 50 per cent of either, according to the patient's tolerance. Although the diet is an important factor, both for attaining cleanliness of the bowel and for giving the patient a fighting reserve, other means of emptying the colon have been found expedient. Depending on the amount of obstruction present, castor oil in variable doses of from 30 to 60 cc. is given by mouth in some cases. Twelve hours later, cleansing enemas of a physiologic solution of sodium chloride are given, which are repeated every twelve hours until twenty-four hours before operation. Such preparation takes from three to five days, depending on the amount of obstruction produced by the lesion, its situation in the colon and the general condition of the patient.

If barium has been used in the diagnosis of the lesion of the colon, it must be removed thoroughly. In the diagnosis of lesions of the colon by means of the x-rays, it is more important whenever possible to use thin barium and to wash it out thoroughly by enemas as soon as the roentgen examination has been made. A flat roentgen picture of the abdomen made from twenty-four to forty-eight hours after barium has been given eliminates the danger of sending a patient to the operating table with barium in the bowel. During the first twelve of the last twenty-four hours preceding the first operation, divided doses of camphorated tincture of opium are given by mouth. These serve to allay peristalsis and to quiet the patient in general. Patients are urged to drink much liquid up to twelve hours before operation. During the last twelve hours, the patient is allowed absolute rest; everything is done for his comfort and composure.

The day after the colostomy has been done, irrigations of the lower portion of the bowel which contains the tumor are begun. A physiologic solution of sodium chloride is used, and the irrigations are continued until forty-eight hours before the second stage, or resection. During the last forty-eight hours before the resection, aspiration of the lower segment by section is carried out both from the colostomy opening and from the rectum; it is done several times a day to prepare a dry operating field. The patient again is placed on the carbohydrate diet for twenty-four hours before the resection, and a simple cleansing enema of the portion of the bowel above the colostomy is given the night before operation to prevent gross fecal soiling at the time of operation. Before discontinuing irrigations of the lower portion, the rectum is examined digitally to determine whether or not it is empty.

The patient is observed carefully during the preoperative preparation in an effort to estimate surgical risk and to avoid complications, if possible. Not only is the lesion in the bowel examined carefully by

digital, proctoscopic and, whenever advisable, by roentgenologic methods, but the heart, blood pressure and lungs are carefully examined. Electrocardiograms are made whenever they are thought to be necessary. Renal function is estimated by phenolsulphonphthalein and studies on the blood urea. In older men with hypertrophied prostates and residual urine, particularly if there are rectal lesions, lavage of the bladder is instituted in an effort to avoid an ascending pyelocystitis. A careful note is made of the quantitative output of urine, and particular mention is made of any sign of edema of the extremities. This is especially significant in checking the not infrequent development of postoperative nephrosis. If noted early, the development of this condition into a serious complication usually can be avoided.

An additional measure, which we trust will have an important bearing on the successful management of these cases in the future, is intraperitoneal vaccination against infection of the peritoneal cavity by the use of a mixed vaccine prepared after the methods of Herrmann, who has used it extensively in experimental work. Experience with this type of medication has been too short to warrant an opinion as to its value, but we hope to be able to report more favorably on it in a future communication.

Rehabilitation after resection of a malignant tumor and establishment of colostomy is an important adjunct in the management of the patient. An effort to regulate the time of fecal evacuation from the colostomy opening, as well as to aid the establishment of formed stools by making the patient somewhat constipated, is necessary. The patient is advised, therefore, to eat at regular intervals, to include constipating foods in his diet and to avoid drinking between meals. Another significant consideration is the choice of the colostomy bag. It must be as inconspicuous as possible, should not create a vacuum by its pull on the exposed part of the colostomy, must be easily cleaned and should be relatively inexpensive.

The general acceptance of colostomy for growths in the left colon is perhaps one of the greatest advances in surgery of the colon in the last two decades. Whether the colostomy should be permanent when growths in the upper part of the rectum and sigmoid may be removed safely or whether an anastomosis should be made to reestablish continuity of the bowel is still a question. Although the technical maneuver is feasible, there are surgeons who argue, with considerable logic on their side, that growths in the sigmoid should be treated like growths in the rectum, with colostomy and extirpation of the segment of bowel below it. Usually, in cases in which colostomy is employed, because of the preliminary cleansing of the bowel and irrigation of the local growth to overcome obstruction, we have been able to leave the

bowel intact until the sixth day or longer; then, as gas begins to accumulate and the patient becomes uncomfortable, puncture is made with the cautery to relieve the tension. Subsequently, after healing is insured, the bowel is divided across its entire lumen. Following each operation it has been our custom, satisfactorily carried out, to insist on abstinence from any food or drink by mouth for seventy-two hours or longer. Good evidence that the gastro-intestinal tract is functioning satisfactorily and that infection is not taking place is the patient's ability to expel flatus. After this, administration of liquids by mouth is begun, and gradually the diet is increased. Adequately prepared patients are surprisingly free from gas in the postoperative period, and it is our experience that much of the discomfort following abdominal operations, on both the colon and the viscera, is the result of feeding the patients too early in convalescence. In colonic cases, subcutaneous administration of physiologic solution of sodium chloride or of solution of dextrose (d-glucose) is begun postoperatively, and a continuous flow at the rate of 100 cc. each hour up to 2,000 cc. in twenty-four hours is administered over the necessary period of time. Once the colostomy is done, irrigations are begun through-and-through, so as to alleviate further the local condition and to assist in adequate preparation for the subsequent resection. Usually the interval between the first and second stages of the operation has been from ten to sixteen days.

The selection of the type of operation is not entirely standardized, and the type of operation varies considerably with the half of the colon which is operated on, but the institution of drainage and the principle that most resections of the colon should be graded procedures is unquestionably a step in advance. Although it has been our aim in this group of cases to select the most radical surgical procedure compatible with the general condition of the patient, in the main, graded maneuvers rather than single-stage operation have been done. The graded operation is advantageous from many standpoints and in our hands has been instrumental, we believe, in a most satisfactory lowering of mortality.

To evaluate an aseptic technic for the removal of carcinoma of the colon is difficult. It is only one and one of the least significant steps in the development of surgical treatment of malignant conditions of the gastro-intestinal tract and yet it offers many advantages, and any procedure which accomplishes removal of intestinal carcinoma without opening the intestinal lumen, and with satisfactory functional results, merits consideration. To accomplish successfully a blind resection one must minimize the danger of infection of the peritoneum, which is the main cause of failure in gastro-intestinal surgery, and many simple methods available today emphasize the ease of its accomplishment and make its allocation among other maneuvers more ready.

Each of the two segments of the colon demands a definite technical operation, even though the principle of performing removal of the carcinoma in a graded procedure is adhered to. It has been our custom to attack right-sided colonic carcinomas by first making an aseptic ileocolostomy, and then in about two weeks removing the right half of the colon and from 30 to 35 cm. of the ileum. We believe the end-to-side transplantation of the ileum into the transverse segment of the colon is the most satisfactory type of procedure in this situation, and it can be accomplished easily and with satisfactory functional results by any of the aseptic methods popular today. The dangerous part of this operation is the secondary resection. It, likewise, may be accomplished in a clean manner, but it is more likely to be followed by peritonitis because of contamination from the necessary mobilization of the infected growth.

Colocolostomy or ileocolostomy and subsequent resection of the ascending colon and a portion of the transverse colon is the operation of choice for carcinomas of the transverse colon, unless one resorts to an obstructive operation. The latter type of operation in our service has proved exceptionally useful. We believe that in the majority of cases in which there is little obstruction and in which adequate preoperative measures have been instituted to cleanse the bowel and in this manner to eliminate a certain amount of infection, an obstructive operation may be done. In these cases one may resect the transverse colon or, indeed, any other mobile segment of the bowel and may leave on a clamp much more satisfactorily than by doing the old-time exteriorization procedure of Mikulicz. For this Mikulicz procedure we heartily advocate the substitution either of this obstructive resection or of drainage and at a second stage resection and reestablishment of the continuity of the bowel. On our service, the Mikulicz procedure practically has been abandoned except in a small group of cases of elderly patients who have small, scirrhous carcinomas of mobile segments of the large bowel which readily may be brought outside the abdomen without any preliminary measures of mobilization. In obstructive resection or colostomy and subsequent resection, one avoids the disadvantages of the Mikulicz procedure, for in the former there is no question of implantation of cancer cells in the cut surfaces of the abdominal wound, and more widespread dissection of lymph nodes and removal of the tissues contiguous to the growth is made possible. In cases of carcinoma below the transverse colon and splenic flexure, colostomy and subsequent removal is most advantageous in practically every case. The question of reestablishment of the lumen of the bowel depends on the height of the growth in the left side of the colon. Below the middle of the sigmoid, there is without question a disadvantage in joining again the cut ends of the bowel.

The question of operability, likewise, is not always easy to decide. Obviously, hepatic metastasis rules out radical operation except in an occasional case in which a small growth may be resected, by a simple maneuver, to relieve the patient of a local malignant growth. This happens infrequently and, for all practical purposes, may be forgotten. However, the question of inoperability, because of local conditions attendant on attachment to surrounding structures, is frequently perplexing. If the growth is free and movable and may be removed with or without restoration of the lumen of the bowel, the problem is simple, but if the growth is attached to the parietal peritoneum, to the small bowel or, as it occasionally is, to some other viscus which may be sacrificed without too much operative risk, the question as to the advisability of double resection, or resection and some additional operative maneuver, is not easily answered. More often than not, growths which are attached to the lateral parietal peritoneum have penetrated through the peritoneum and occasionally have formed definite pockets which will be ruptured by the slightest operative manipulation to determine the mobility and fixation of the segment of bowel. Many times we have been driven to resect a growth which had become attached to the parietal peritoneum and which had penetrated, but the penetration was not recognizable until the finger slipped easily into a small pocket during the examination. Mortality is relatively high following this accidental rupture of an abscess because of the direct contamination, and one of the greatest factors in the reduction of operative mortality will be the recognition of growths which are irremovable before some such accidental discovery forces the surgeon to perform resection. Under obstructive conditions the region of the growth becomes highly infective. Infection may take place either from increased permeability of the wall of the bowel or from direct invasion of bacteria through the broken mucosa at and around the large, ulcerating, infected, penetrating and attached growth, which may or may not have an abscess form around it.

Advanced growths which have attending complications due to their fixation, immobility and perforation of the wall of the bowel demand the exercise of meticulous judgment to decide not only whether they are amenable to radical resection but also whether palliative operation is indicated. Fixation in carcinoma of the colon, in the vast majority of instances, is due to inflammatory reactions rather than to direct invasion. The graded operation permits recession of this inflammatory reaction in many instances, with subsequent lessening of the fixation. There is then the likelihood that more radical procedures for removal of the local growth and its offending gland-bearing areas may be instituted with a most satisfactorily small operative mortality.

The choice of anesthetic in colonic cases is not unimportant. Miles, years ago, advocated spinal anesthesia in performing his abdomino-

perineal resection for carcinoma of the rectum, but it has not been universally adopted because of the dislike of general surgeons, as a class, for spinal anesthetization. In our service, during the last two years, we have employed spinal anesthesia as a routine for colostomy and the subsequent resection of all carcinomas of the rectum and for the drainage operation and removal of resectable carcinomas of the colon. The advantages of this procedure have been manifold, and we are convinced that it has had a satisfactory effect on the statistics of immediate operative mortality. Most infrequently we have found it necessary to complement the spinal anesthesia with nitrous oxide, oxygen or ethylene. The only contraindication to the use of spinal anesthesia, to which we have adhered, has been a marked lowering of the systolic blood pressure. The blood pressure is sustained throughout the operation by the administration of ephedrine. Despite an occasional reaction while the patient is on the operating table, we have no inclination to discontinue the use of spinal anesthesia. We feel confident that although the margin of safety may be smaller than that in the routine administration of anesthesia by inhalation, the freedom from pulmonary complications and the relaxation and additional ease in operating warrant the employment of this procedure in this type of case. The operative mortality is necessarily higher in this group than it is in other types of cases, and the risk justifies employment of more radical measures if they are of even slight advantage.

A REVIEW OF ABDOMINAL SURGERY*

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GALLBLADDER

Moynihan¹ found that infection began in the outer coats of the gallbladder in 63 of 81 cases of cholecystitis. In 18, the inner coats were primarily involved. Infection may reach the outer coats by direct extension from the liver, by means of the lymphatics communicating directly between the liver and gallbladder or by involvement of the peritoneal surface as a consequence of disease in an adjacent organ. In cases of infection from within, the ascending route is followed more frequently than is realized. Cholecystitis as a rule is only a part of an infection which has its origin elsewhere. Hepatitis is commonly, if not always, present, and is almost certainly of earlier origin than the inflammation of the gallbladder. Moynihan stated that sufficient regard has not been paid to the spleen as an infective agent. In some cases with recurrent stones and with marked infection in the common bile duct, the spleen may be a causative factor, and splenectomy in such cases may be indicated.

Moynihan stated that the presence of all or most of the symptoms of cholecystitis over a period of weeks or months is sufficient indication for operation. The symptoms, he emphasized, are flatulence and fulness after meals, epigastric discomfort, pain, sudden nausea, acidity, water-brash and sallow complexion. The Graham-Cole procedure is a valuable diagnostic aid, because the concentration of bile has been shown to be checked at times when the external appearance of the viscus is only slightly altered. If inaugural symptoms are present and the cholecystographic shadow is absent or delayed, operation may be performed.

* Submitted for publication, May 7, 1929.

1. Moynihan, Berkeley: Mitchell Banks Memorial Lecture on the Gall-Bladder and Its Infections, Brit. M. J. 1:1, 1928.

Moynihan many times has hesitated to take the gallbladder out in cases of inveterate mild dyspepsia; when he has not done so, he has been compelled to operate later and has had good results. He was of the opinion that the gallbladder should be removed more frequently than is now being done.

Wilkie² of Edinburgh also stressed the importance of early surgical intervention in disease of the gallbladder. In cases of flatulent dyspepsia, in which the gallbladder seems implicated, he advised removal.

[COMPILERS' NOTE.—Recent studies of the functions of the gallbladder demonstrate that it is not merely a vestigial organ, and although its loss is well tolerated in man, we believe that the best indication for its removal is the clinical history and especially the presence of colic. Patients who give such a history usually will be relieved of symptoms by removal of the gallbladder even in the absence of any grossly demonstrable pathologic lesion. Patients with symptoms of mild dyspepsia and indefinite complaints relative to the upper part of the abdomen are not always cured by removal of a gallbladder which appears normal. The Graham-Cole procedure is a good diagnostic aid, but it should not be used as an indication for cholecystectomy in the absence of a good clinical history of disease of the gallbladder. We believe, as Moynihan and Wilkie have indicated, that the best results are obtained by operating as soon as the diagnosis is made.]

Wilkie,³ in an experimental study, concluded that infection in the gallbladder precedes the common hepatic changes seen in cholecystitis. He interposed omentum between the liver and gallbladder in rabbits and produced cholecystitis by injecting streptococci obtained from cystic lymph glands of man which drained diseased gallbladders. In cases in which the omentum had been interposed between the gallbladder and liver, the liver remained grossly and microscopically normal. In the control animals, definite localized hepatitis was produced.

[COMPILERS' NOTE.—More or less well defined localized hepatitis is such a constant occurrence in cholecystitis that its presence may be used as an indication of disease of the gallbladder even in the absence of marked pathologic changes in the gallbladder itself. We are, nevertheless, inclined to the view that the primary lesion is most often in the gallbladder, and that the localized hepatitis is secondary.]

Illingworth,⁴ in 100 cases in which operation had been done, noted the frequency of intramural infection of the gallbladder and that sterile bile rather commonly is found. He concluded that cholecystitis is a

2. Wilkie, D. P. D.: Personal communication.

3. Wilkie, A. L.: The Significance of Hepatitis in Relation to Cholecystitis: An Experimental Study, *Brit. J. Surg.* **16**:214, 1928.

4. Illingworth, C. F. W.: Types of Gall-Bladder Infection: A Study of 100 Operated Cases, *Brit. J. Surg.* **15**:221, 1927.

blood-borne infection and that ascending infection, or infection from the liver, is the exception rather than the rule.

Bacteriology.—Wilkie⁵ concluded that cholecystitis is a blood-borne streptococcic infection of the walls of the gallbladder. He made cultures of the whole thickness of the wall of the gallbladder and found that growth did not result as a rule, whereas cultures from the submucosa and outer coats, leaving the mucosa intact, gave growths of streptococci in 42 per cent of cases. Bile inhibited the growth of streptococci. The cystic lymph node in cholecystitis gave a growth of streptococci in 86 per cent of cases.

In only 6 per cent of cases was *Bacillus coli* recovered from bile; in only one case was it recovered from the cystic lymph node and in this case probably there was contamination from bile.

A suspension of streptococci in physiologic solution of sodium chloride was injected into the lumen of the gallbladder in rabbits and did not produce change. However, intramural injection of the suspension produced progressive chronic cholecystitis, and the organism readily was recovered. Intramural injection of the suspension of streptococci, after the cyst duct was ligated, produced chronic empyema with marked intramural changes. Calculi were produced in both types of intramural injection. Repeated intravenous injections of the streptococci gave progressive chronic cholecystitis with formation of cholesterol stones. Intramural infections of the gallbladder without ligation of the cystic duct produced only stones of cholesterol, but when the cystic duct was ligated, the stones produced were of calcium and cholesterol. The intramural injections gave pathologic changes which resembled in every way those found in diseased gallbladders in man.

Wilkie² emphasized the importance in making bacteriologic studies in disease of the gallbladder of making cultures from the cystic lymph node at the neck of the gallbladder. In 100 cases of disease of the gallbladder including early cases with practically no change in the appearance of the gallbladder, 84 cystic lymph nodes gave a pure culture of streptococci.

[COMPILERS' NOTE.—One cannot draw definite conclusions as to the rôle played by bacteria in producing cholecystitis by bacteriologic studies of the gallbladder and bile. Judd, Mentzer and Parkhill,⁶ in 200 cases, obtained 14 per cent of positive cultures from the bile of the gallbladder. Positive cultures were most frequently obtained from light colored, grainy, purulent or blood-tinged bile. Bile of normal appearance,

5. Wilkie, A. L.: The Bacteriology of Cholecystitis: A Clinical and Experimental Study, *Brit. J. Surg.* **15**:450, 1928.

6. Judd, E. S.; Mentzer, S. H., and Parkhill, Edith: A Bacteriologic Study of Gallbladders Removed at Operation, *Am. J. M. Sc.* **173**:16, 1927.

including concentrated dark bile, was usually negative. Forty-nine per cent of positive cultures were obtained from the wall of the gallbladder and 31 per cent from gallstones. Rosenow, many years ago, obtained a much higher percentage of positive cultures. This may be due to the fact that chronically diseased gallbladders were not removed as frequently then as now.]

Etiology.—Sherwood⁷ reviewed a series of 200 consecutive cases of diseases of the biliary tract occurring in the last four years. The pathologic material included other cases in the same hospital studied by Denton. He examined 400 gallbladders and characterized the lesions of the biliary tract as primarily mechanical and circulatory rather than infectious disturbances.

In Sherwood's experience, by far the greater number of disturbances of the biliary tract which may be treated successfully by the surgeon, with the greatest relief and satisfaction to the patient, are those which have their basis in obstruction to the normal flow of bile through the system of ducts. The most common cause of obstruction is the presence of stones. Stones in the extrahepatic ducts are the most serious, the gravity of the condition depending on the completeness of the occlusion. The presence of stones in the gallbladder may or may not be accompanied by symptoms or appreciable pathologic changes. Such stones often appear to be harmless foreign bodies although invariably they are a potential source of trouble and danger. Cultures made from freshly removed gallbladders which contained stones frequently gave negative results, and sections of the walls of the gallbladder did not reveal any of the characteristic changes associated with infection. On the other hand, when pathologic change is easily recognizable, such changes appear to be the result of mechanical and circulatory disturbances. That secondary infection may and often does develop as a result of the presence of stones is not denied. Sherwood believed that a disturbance or unbalance of chemistry in the body, particularly in its relation to cholesterol and metabolism of calcium, must be a significant and primary factor in the etiology of cholelithiasis.

Patients who obtained the most permanent and complete relief following operation were those with cholelithiasis who sought relief because of repeated attacks of biliary colic or because of an acute attack characterized by severe pain in the right upper quadrant of the abdomen. At operation in these cases it was found that almost invariably they were associated with impaction of a stone in the cystic or, more rarely, in the common duct; the underlying pathologic changes were due to mechanical and circulatory disturbances rather than to infection. When infection was present, it seemed to be a complication.

7. Sherwood, W. A.: Surgical Lesions of the Biliary Tract, *Ann. Surg.* 88:178, 1928.

The patients with the least satisfactory results in relief from symptoms were those without stones, who sought relief not because of severe pain or colic but because of vague digestive disturbances, and who did not have more definite pathologic changes than slight fibrosis or involution atrophy. Such changes are the same as may be seen in many other tissues and organs in patients after middle age. Sherwood expressed the belief that such gallbladders should be less frequently removed than has been the practice in many clinics, and that causes for such symptoms should be sought elsewhere. The word, cholecystitis, implies the presence of infection, and Sherwood asks if it always portrays an accurate picture of the most frequently encountered and predominant surgical lesions of the gallbladder.

[COMPILERS' NOTE.—For many years we have been under the impression that not all cases of disease of the gallbladder are due to bacterial infection. A number of years ago, while observing the effects of the intravenous injection of surgical solution of chlorinated soda (Dakin's solution) in animals, Mann was surprised to note its apparent selective affinity for the gallbladder and the production of cholecystitis indistinguishable pathologically from certain cases of chronic cholecystitis in man. This, and more recent studies by Mentzer⁸ and others, have led us to believe that certain groups of diseases of the gallbladder are due to chemical or metabolic disturbances. This view is strengthened by the belief that cholecytic disease is often not a disease of a single organ but of a system and of each person.]

Lyons and Swalm⁹ expressed the belief that many cases in which a positive cholecystogram is obtained by the Graham-Cole method and in which, at operation, a pathologic lesion of the gallbladder is not found, are due to an obstructive catarrhal condition of the cystic duct, which will respond to nonsurgical drainage, which will remain normal and which will give a negative cholecystogram. This is particularly true in cases of low-grade cholecystitis. There is no definite symptomatology in this form of obstruction of the cystic duct and it can be diagnosed only by studies of biliary drainage.

Diseases of the Gallbladder in the Young.—Potter¹⁰ found that pathologic lesions in the biliary tract are much more common in young persons and children than is generally recognized. He reviewed

8. Mentzer, S. H.: Cholesterosis of the Gallbladder, *Am. J. Path.* **1**:383, 1925; A Clinical and Pathologic Study of Cholecystitis and Cholelithiasis, *Surg. Gynec. Obst.* **42**:782, 1926; The Pathogenesis of Biliary Calculi, *Arch. Surg.* **14**:14 (Jan.) 1927.

9. Lyons, B. B. V., and Swalm, W. A.: Obstruction of the Cystic Duct of a Catarrhal Variety, *J. A. M. A.* **90**:833 (March 17) 1928.

10. Potter, A. H.: Gallbladder Disease in Young Subjects, *Surg. Gynec. Obst.* **46**:795, 1928.

226 cases from the literature and added 4 of his own in which disease of the biliary tract existed in children up to 15 years of age. He cited 2 cases of stones in the common duct in fetal life (6 and 8 months, respectively). In the entire series, gallstones were present in 140 cases, cholecystitis with stones in 44 cases, cholecystitis without stones in 59 cases and cholecystitis with jaundice in 30 cases. Stones in the cystic duct were found 14 times; in the common duct, 13 times. Hydrops of the gallbladder was found 18 times and infection of the gallbladder 43 times. There were 2 cases of malignant disease of the gallbladder in patients aged 4 and 15 years, respectively. Acute cholecystitis is relatively common in the series.

Potter believed that etiologically, and in order of their importance as causative agents in diseases of the gallbladder, are the following: influenza, appendicitis, scarlet fever, diphtheria and infections of the digestive tract regardless of origin.

Operations.—DeCourcy¹¹ reported a series of 400 operations on the gallbladder in which cholecystectomy yielded better operative results than cholecystostomy. He reviewed this subject and found that, in general, recognition is given the fact that symptoms are only too likely to persist after simple drainage of the gallbladder, even if there is no actual recurrence of the disease. Furthermore, an infected gallbladder, if allowed to remain within the abdominal cavity, is a menace to the security of the biliary ducts, pancreas, liver, duodenum and organism as a whole.

[COMPILERS' NOTE.—In most surgical clinics, cholecystectomy is now performed in preference to cholecystostomy in cases of chronic cholecystitis. Concerning the treatment for acute cholecystitis, there is not very uniform agreement. We prefer, whenever possible, to let the acute condition subside and then to remove the gallbladder. Cholecystostomy is done only when some particularly difficult technical procedure presents itself or the poor condition of the patient demands the least dangerous operation. In some jaundiced patients, also, it is advisable to leave in the gallbladder, as it may be useful later if a condition arose which necessitated an anastomosis between the biliary and the intestinal tracts.]

Pribram¹² reported a procedure he had used in about 200 cases of cholelithiasis, which has been successful in the most complicated and difficult cases and which has permitted him to carry out the principle of abdominal closure without drainage. The reasons which usually have

11. DeCourcy, J. L.: Cholecystectomy or Cholecystostomy? *Internat. J. Med. & Surg.* 41:426, 1928.

12. Pribram, B. O.: Mukoklase und drainagelose Gallenchirurgie, *Zentralbl. f. Chir.* 55:773, 1928.

been given against closure without drainage are the danger of a ligature slipping off the cystic duct, secondary hemorrhage and drainage of bile from the hepatic surface. The last mentioned complication is the one most frequently encountered. To avoid this complication, Pribram carries out the following technic: The gallbladder is first drained of all bile by means of suction, and with scissors a longitudinal slit is made in the gallbladder from the fundus to the cystic duct; all stones are removed; the exposed cystic duct is now cut between two ligatures, the mucous surfaces of the gallbladder then are charred by means of the actual cautery and any small hepatic abscesses lying behind the gallbladder are likewise destroyed; cauterization extends through to the serosa of the gallbladder; the two cauterized flaps of the gallbladder are then inverted into the fossa of the gallbladder and the serosal surfaces of the gallbladder are sutured over the fossa.

The method is recommended for those cases of cholecystic disease in which subserous extirpation of the gallbladder is technically impossible because of inflammatory changes in the wall. Raw surfaces in the fossa of the gallbladder thus are eliminated.

Biliary-Intestinal Anastomosing Operations.—Judd and Parker¹³ studied 137 consecutive cases in which anastomosis of the biliary and gastro-intestinal tracts was carried out from 1919 to 1924. There were 34 cases of carcinoma of the pancreas. Contrary to the general teaching, colic with jaundice occurred in 35.29 per cent of these cases, pain with jaundice in 23.52 per cent and colic, pain and jaundice in 2.94 per cent. Thus colic or pain, or both, with jaundice occurred in 61.75 per cent and jaundice without pain in only 38.23 per cent of cases. Intermittent jaundice occurred in 5 of the 12 cases with colic alone. Gallstones were found in only 1 case. Cholecystogastrostomy was the operation of choice in this group, and was performed in 26 of the 34 cases. The average postoperative duration of life was 7.7 months. The relief from jaundice in patients who survived operation was complete and permanent in 63.63 per cent of cases.

Carcinoma of the biliary ducts occurred 9 times in the series. The lesion was situated at the ampulla in 6 cases. Colic with jaundice occurred in 22.22 per cent, pain with jaundice in 44.44 per cent and jaundice without pain in 33.33 per cent of cases. Cholecystogastrostomy was the operation of choice. The average postoperative duration of life was 12.2 months.

There were 14 cases in which it was impossible at operation to determine if the lesion was carcinoma of the pancreas or pancreatitis.

13. Judd, E. S., and Parker, B. R.: Biliary Intestinal Anastomosis for Obstructive Jaundice: Analysis of 137 Consecutive Cases, *Arch. Surg.* **17**:1 (July) 1928.

In this group jaundice without pain was present in 71.42 per cent of cases. Cholecystogastrostomy was again the operation of choice. Of this group, 4 patients are alive; 2 have lived six years; 1, more than three years, and 1 for one year. Eleven cases of pancreatitis are reported. Of these, 6 patients had pain and colic, and 5 did not have pain or colic.

There were 62 cases of stenosis of the biliary ducts. All but one of these patients had been operated on previously. This patient had acute cholecystitis with stones and a dense cicatricial stricture of the duct. In some patients, the trouble appeared immediately after operation, and in others obstructive symptoms did not occur until a number of months following operation. In several cases the stricture probably was due to continuation of the inflammation of the biliary duct, obliterative cholangitis. Pain and colic were common symptoms. In only 3 cases there was no jaundice; in all the others intermittent jaundice of some degree was present. Hepaticoduodenostomy was the operation of choice. Seventeen patients are living and cured more than five years postoperatively; 16 are greatly improved from two to six years postoperatively; 9 are in only fair health; 2 have occasional attacks of pain, chills with fever and jaundice, but little dyspepsia. Partial or complete contraction of the stoma occurred in 7 of the 47 cases in which hepaticoduodenostomy had been performed for stricture. Return of symptoms occurred from one to six months postoperatively. Reconstruction over a tube was carried out in each case. Six patients survived operation; 2 are completely relieved of symptoms three and a half and four years postoperatively; 3 are much improved. One patient, who apparently was recovered from biliary obstruction, died one and a half years after operation from acute gastric obstruction.

Drainage.—Richter and Zimmerman¹⁴ have closed the abdomen without drainage in operations on the gallbladder for over twelve years and are convinced of the safety and of the advantages gained in omitting the drain. They also close without drainage after work on the common duct and after transduodenal choledochotomy as well as after simple cholecystectomy. They usually follow this practice in acutely infected cases as well as in chronic cases and in relatively aseptic cases. They do not regard the spilling of bile or of duodenal contents in the field of operation as a contraindication to primary closure. If there is uncontrollable oozing, or if in operations on the common bile duct accurate closure of the duct is not possible or some other special contraindication exists, drains are used. Richter and Zimmerman have made primary closure in 262 operations on the biliary tract.

14. Richter, H. M., and Zimmerman, L. M.: Closure of the Abdomen Without Drainage After Operations Upon the Bile Ducts, *Ann. Surg.* 88:187, 1928.

Their report is based on 418 operations done in consecutive cases of disease of the biliary tract. Cholecystectomy was done in 323 cases 65 times with additional work on the common duct and 25 times associated with some other major abdominal surgical procedure. In the 232 operations of cholecystectomy, the wound was drained in 70 and closed primarily without drainage in 253 cases. Simple cholecystectomy with primary closure was done 204 times with 2 deaths, an average mortality rate of 0.98 per cent. One death was due to acute pancreatitis, the other to pulmonary embolism. The average mortality in all the cholecystectomized cases, including those with work on the common duct, or other major operative procedures, was 3.39 per cent. The percentage of fatalities is higher in the groups in which drainage was allowed than in those in which it was not provided for; the explanation is that the most difficult cases are those in which drainage most often is required. The common bile duct was operated on 84 times in this series: in 55 cases with drainage and in 29 with primary closure. Of the group of 55 patients, 10 died, and there were 2 deaths in the 29 cases without drainage. There were 23 deaths in the entire series, an operative mortality of 5.5 per cent. Sixteen of the 23 deaths were in cases in which drainage was allowed, whereas only 7 deaths occurred in the cases without drainage. Among the cases in which drainage was not instituted there was only 1 death from peritonitis. In this case cholecystectomy and transduodenal exploration of the common bile duct was done.

The advantage of omitting the drain is that the postoperative discomforts are minimized, the incidence of infection and hernia is less and the period of convalescence is shortened. The frequent escape of bile seen after operation in which the incision is drained is not seen if the drain is omitted. Two cases are cited in which operation was done elsewhere; because of technical errors a large amount of bile accumulated in the abdominal cavity, remained some time and apparently was well tolerated.

Wangensteen,¹⁵ as a result of an experimental and clinical study and an extensive review of the literature pertaining to the question of drainage in operations on the gallbladder, concluded that all wounds in cholecystectomy should be drained.

[COMPILERS' NOTE.—While certain rules can be laid down for either draining or not draining in surgical cases, in the final analysis the question remains one for each surgeon to decide from his own experience. We have closed the abdominal wound without drainage in a number in which cholecystectomy was performed. Each case must be decided indi-

15. Wangensteen, O. H.: Should the Gall-Bladder be Removed Without Drainage? *Ann. Surg.* 84:821, 1926.

vidually, and if the drain safely can be omitted, we find that the patient has a smoother and more rapid convalescence. We always institute drainage after surgical procedures on the common bile duct.]

Anomalies.—Bower¹⁶ reported a case of a man, aged 50, who was operated on because of severe pain in the upper right portion of the abdomen. The diagnosis was acute pancreatitis or perforated duodenal ulcer. At operation, the liver was found to be entirely without a left lobe and a gallbladder or fissure was not present; extrahepatic ducts could not be definitely demonstrated. The head of the pancreas was swollen and firm.

An abstract of previously reported cases is given, which included 13 cases of absence of the gallbladder and all ducts, 14 cases of absence of the gallbladder, cystic and common bile ducts and 31 cases of absence of the gallbladder and cystic duct. Other anomalies are also briefly discussed.

[COMPILERS' NOTE.—We have seen a case of congenital absence of the gallbladder which was discovered at necropsy in a patient who during life had not had manifestations of cholecystic disease. The common duct was only slightly larger than normal. At operation, one sometimes has to search carefully for a gallbladder which has been totally destroyed as a result of chronic inflammation. Often only a little bit of shrivelled scar tissue remains.]

Cholecystography.—Dick and Wallace¹⁷ presented two cases with untoward reactions following the intravenous injection of sodium tetraiodophenolphthalein for cholecystography. In one, acute hemorrhagic pancreatitis followed immediately the injection of the dye. In another, jaundice developed following the use of the dye, and in a third case death resulted from the oral administration of the dye in a young jaundiced patient.

Experimentally, normal bile to which sodium tetraiodophenolphthalein was added was introduced into pancreatic ducts and it produced acute pancreatitis. From this it might be inferred that in the presence of a stone of the common bile duct a similar reflux into the pancreatic ducts of bile containing the salt might occur and cause pancreatitis. In cases of obstructive jaundice, small quantities of sodium tetraiodophenolphthalein were found in the pancreatic juice, and from this Dick and Wallace concluded that injury to the pancreas is possible when the dye is used in cases of obstructive jaundice. They believed

16. Bower, J. O.: Congenital Absence of the Gall-Bladder, *Ann. Surg.* **88**:80, 1928.

17. Dick, B. M., and Wallace, V. G. H.: Cholecystography: Toxic Effects of the Dyes: A Clinical and Experimental Study, *Brit. J. Surg.* **15**:360, 1927-1928.

that in the presence of the hepatic injury that is found in obstructive jaundice, the dye is more toxic in its effect than when the livers are not so injured.

[COMPILERS' NOTE.—Mild untoward reactions such as nausea, vomiting and purging occasionally follow the administration of the salts of bromine and iodine used in cholecystography. Severe reactions fortunately are rare. Kirklin and Kendall¹⁸ have recently prepared a new compound, di-iodo-di-ethyl-ether of di-salicylphthalein, which is administered orally in the form of a 10 per cent aqueous solution of its sodium salt. The drug is less toxic than those in general use.]

FALCIFORM LIGAMENT

Schmieden and Peiper¹⁹ studied the development, comparative anatomy, histology and pathology of the ligamentum teres hepatis. They found that it reaches its highest state of development in man. It is not a suspensory ligament of the liver, but together with the lateral umbilical ligaments and the fascia umbilicalis, all of which are closely interwoven in the region of the umbilicus, the falciform ligament forms a support for the anterior abdominal wall. The ligamentum teres hepatis contains a number of blood vessels and lymph channels and also a great deal of smooth muscle and apparently is capable of lengthening and shortening under nervous control, although this has not been definitely demonstrated. The authors have seen two cases in which pathologically produced shortening of the ligament caused symptoms in the upper part of the abdomen which were relieved by dividing it. They were of the opinion that this shortening is due to a chronic inflammatory process. The ligament furnishes a bridge between the retroperitoneal tissues and the anterior abdominal wall. In acute pancreatitis, it is often endematous and contains areas of fat necrosis. It is suggested that the umbilical colic in appendicitis in children may be due to spasm of the smooth muscle of the ligament.

The falciform ligament also is important as a pathway for the spread of carcinoma. Metastasis has been found in the ligament in carcinoma of the stomach and liver. Together with the umbilical ligaments, the falciform ligament may furnish the route by which carcinoma of the rectum metastasizes to the liver. In primary malignant tumors of the umbilicus, as much of the ligament should be excised as possible. The vessels of the ligamentum teres hepatis form an anastomosis with those of the abdominal wall on one side and with the portal

18. Kirklin, B. R., and Kendall, E. C.: New Iodine Compound for Cholecystography, *Radiology* 9:205, 1927.

19. Schmieden, Viktor, and Peiper, Herbert: Die Chirurgie des Ligamentum teres hepatis, *Arch. f. klin. Chir.* 152:393, 1928.

vein on the other. This is of significance in cirrhosis of the liver, and Talma's operation, therefore, should be done not above but below the umbilicus in order to avoid interfering with the natural compensatory circulation furnished by the ligamentum teres hepatis.

[COMPILERS' NOTE.—The falciform ligament has wide normal variations in form, structure and vascularity. We never have hesitated to divide the ligament when doing so would give better exposure of the field of operation. The advantages of dividing it are particularly evident in operations on the biliary tract. We have always been careful to reunite the cut ends of the ligament before closing the abdominal wound and are not aware of any ill effects resulting from this procedure.]

PANCREAS

Schmieden and Sebening²⁰ reviewed a series of 1,510 cases of acute pancreatic necrosis occurring since 1918. In this series, 980 cases were in women and 520 in men. Operation was performed on 1,278 patients. There are numerous theories as to the cause of acute pancreatitis, but diseases of the biliary tract are of greatest significance in its etiology. Of 1,278 cases in which operation was performed for acute pancreatic necrosis, there was disease of the biliary tract in 894 (69.8 per cent). In 31 cases of acute pancreatitis associated with gallstones the authors found stones in the ampulla in 7. Schmieden and Sebening reported 38 cases of pancreatitis after operations on the biliary tract, of which 24 followed cholecystectomy. A preoperative diagnosis of pancreatitis is not often made. The diastase reaction of Wohlgemuth is of diagnostic value. A correct diagnosis was made in 21.8 per cent and a probable diagnosis in 17.5 per cent of all the patients operated on. The incorrect diagnosis most frequently made was acute cholecystitis.

Early operation is imperative, as 95 per cent of patients not operated on die. In Schmieden and Sebening's series, the operative mortality was 51.2 per cent. In addition to instituting drainage, significant lesions of the biliary tract should be remedied. In the patients who recover from the operation, the prognosis is good. Of 624 patients who lived, only 26 had recurrences. There may be a temporary diminution in dextrose tolerance; diabetes followed in 18 cases of this series. In 6 cases, chronic pancreatitis developed.

Chronic pancreatitis is generally a medical problem. The condition is hard to recognize even with the abdomen open, as the size and consistency of the gland vary greatly under normal conditions and during different phases of digestion. It is difficult to distinguish pancreatitis from carcinoma. Of a series of 308 patients, 127 had jaundice.

20. Schmieden and Sebening, W.: *Chirurgie des Pankreas*, Arch. f. klin. Chir. 148:319, 1927.

A series of 20 cases of pancreatic stones is reported, 11 of which were removed at operation. All these patients recovered. Of the 20 cases of pancreatic stones, only 2 were demonstrated by the roentgen rays. One hundred and twenty-eight pancreatic cysts are reported, most of which were drained to the outside; a few showed anastomosis to the gallbladder or intestinal tract. Operation in traumatic injury of the pancreas aims to convey the secretions to the outside.

Coenen²¹ has interested himself in a clinical investigation to determine in which cases of acute pancreatic necrosis drainage of the common bile duct, without incision and drainage of the pancreas, is indicated. Unfortunately, the anatomic and physiologic relationship of the biliary and pancreatic ducts is not such that in the majority of cases the toxic syndrome of pancreatic necrosis can be attributed to the presence of bile in the pancreas. Coenen expressed the belief that the common bile duct should not be drained primarily in every case of acute pancreatitis, since this method would bring relief only in those cases in which the pancreatic necrosis originated from the penetration of bile into the pancreatic system. Pancreatitis originating in other ways would not be affected by drainage of the choledochus.

In acute pancreatitis any unnecessary delay in instituting a surgical procedure may seriously handicap the chances of a patient's recovery. Free incision of the diseased pancreas and drainage with gauze strips and rubber tubing are of value in acute pancreatitis.

An absolute indication for drainage of the choledochus may be said to exist, if on examination of the biliary system an associated cholecystitis and cholelithiasis is found to be present. A relative indication for drainage of the choledochus exists if the common bile duct is dilated, or if cloudy bile is aspirated from the common bile duct in cases of pancreatic necrosis. In cases of traumatic pancreatic necrosis drainage of the common bile duct should be instituted only when the common duct is injured.

Grassberger²² studied quantitatively the pancreatic ferments in the blood in diseases of the pancreas, paying especial attention to those patients with gastric or duodenal ulcer penetrating into the pancreas. He investigated especially the atoxyl resisting lipases which are specific to the pancreas. There is no method as yet for differentiating the diastase of the pancreas from that of the salivary glands. Grassberger showed that pancreatic ferments in the blood vary but little under normal conditions and after operations on abdominal organs other than the

21. Coenen, H.: Zur Indikationsstellung der Gallengangsdrainage bei der Pankreasnekrose, *Zentralbl. f. Chir.* **55**:900, 1928.

22. Grassberger, A.: Fermentuntersuchungen im Blut bei Pankreaserkrankungen mit besonderer Berücksichtigung des in das Pankreas penetrierenden Magen-Duodenalulcus, *Deutsche Ztschr. f. Chir.* **210**:293, 1928.

pancreas. In a series of gastric and duodenal ulcers, he was unable to determine whether or not they had penetrated into the head of the pancreas by a study of the ferments in the blood. In acute disease of the pancreas superimposed on a chronically diseased organ there is an increase in the pancreatic lipases in the blood.

Bernhard²³ was able to demonstrate hyperglycemia in pancreatic diseases. In mild cases, 50 Gm. of dextrose is given by mouth and even those patients with only slight pancreatic necrosis showed a delayed curve of blood sugar. The method is of value in distinguishing between disease of the biliary tract and pancreas in certain mild, obscure cases. The hyperglycemia is due probably to decreased production of insulin, and the administration of insulin to the patient is indicated. Bernhard was of the opinion that diseases of the pancreas are a more frequent cause of symptoms referable to the upper part of the abdomen than is generally realized.

[COMPILERS' NOTE.—The diagnosis of chronic pancreatitis, even with the abdomen open, is not always easily made, nor can its degree be accurately measured. Chronic pancreatitis does, however, occur frequently in association with chronic cholecystitis and seems to be a frequent cause of the continuation of symptoms following cholecystectomy. Patients with pancreatitis may continue to have symptoms for from several months to a year or more after operation. In giving a prognosis, it is important to bear this fact in mind.

In excising a gastric ulcer that is adherent to the pancreas, or in doing a resection for gastric ulcer or carcinoma of the stomach, we frequently have been forced to resect a small portion of the pancreas. Occasionally when this has been done a little pancreatic fluid will drain for a time. In all our cases, however, healing has been spontaneous and there have been no untoward effects.

The problem presented by acute pancreatic necrosis is by far the most serious one in diseases of the pancreas. Early operation is imperative, a procedure which sometimes is handicapped by the difficulty in making the diagnosis. Occasionally a true pancreatic abscess forms which may work its way to the anterior abdominal wall. We have seen this occur preoperatively and also following operations on the biliary tract.]

SPLEEN

Spence²⁴ suggested that purpura hemorrhagica is a disease of the whole reticulo-endothelial system and that three different types exist depending on the part involved and the extent of involvement. Splenec-

23. Bernhard, F.: Ueber die Hyperglykaemie bei akuten Pankreaserkrankungen, *Deutsche Ztschr. f. Chir.* **212**:209, 1928.

24. Spence, A. W.: The Results of Splenectomy for Purpura Haemorrhagica, *Brit. J. Surg.* **15**:466, 1927-1928.

tomy, it is known, brings about a cure in some types of purpura hemorrhagica, and in other types it is not of value. This may be explained by the fact that probably the underlying pathologic cause is elsewhere in the reticulo-endothelial system and not in the spleen in these cases in which splenectomy is not of benefit.

The three types described by Spence are: first, those in which the whole reticulo-endothelial system is uniformly affected. The diseased megakaryocytes produce defective platelets which are destroyed in excess by a diseased spleen as well as by the remainder of the reticulo-endothelial system. In these cases, splenectomy gives poor results. The second type are those cases in which the spleen is chiefly affected and the platelets are destroyed by the diseased spleen. Compensating for this rapid destruction of platelets, the megakaryocytes are overworked and are stimulated to produce defective platelets. When the spleen is removed, the rapid destruction of platelets ceases and the bone marrow is enabled to recover and to produce normal platelets. In this type, splenectomy is of great service. The third type are those cases in which the injury is to the bone marrow and extrasplenic reticulo-endothelial system rather than to the spleen. Obviously, splenectomy in this type is useless.

Green²⁵ stated that splenectomy for thrombocytopenic purpura hemorrhagica is a purely empiric procedure and is based on the knowledge that splenectomy produces an increase in the blood platelets or thrombocytes. Investigators have shown that splenectomy causes this increase of platelets immediately, and in large numbers, and that they appear in increasingly greater numbers each day, reaching their greatest height from the tenth to the fourteenth day. Following this they subside to the normal figure in from three to four weeks. Little is known of the etiology or pathology of thrombocytopenic purpura, and differentiation from other diseases of the blood is often difficult. Werlhof first separated purpura hemorrhagica from other hemorrhagic diseases in 1731.

The essential characteristics of purpura hemorrhagica are: marked decrease of platelets, normal coagulation time, delayed bleeding time, no retraction of the clot and no variation in the cellular elements of the blood. Unless these factors can be demonstrated, one should hesitate before calling a given condition purpura hemorrhagica and splenectomy should not be done.

Brill and Rosenthal first associated thrombocytopenic purpura with the reticulo-endothelial system. The cells of this system are found in the blood sinuses of the spleen, the sinuses of the lymph nodes, the

25. Green, T. M.: Splenectomy for Thrombocytopenic Purpura Hemorrhagica, *Internat. J. Med. & Surg.* **41**:487, 1928.

capillaries of the hepatic lobules and in the capillaries of the bone marrow. Some of these cells also are observed wandering throughout the connective tissues of the body and also, clustered about the capillaries. These cells are known as Rouget cells and seem to exert definite control over the passage of the cellular elements of the blood through the capillary wall.

In 1916, Kaznelson advocated splenectomy for this condition on the assumption that the disease was due to excessive destruction of the blood platelets from overactivity of that portion of the reticulo-endothelial system situated within the spleen. When other portions of this system are at fault, as in Gaucher's disease, splenectomy is useless since the affected part of the reticulo-endothelial system lies within the lymph nodes and bone marrow. Focal infection has been given as a causative factor in the dysfunction of the reticulo-endothelial system. In the application of the tourniquet, petechiae do not appear in acute cases and do appear in the chronic cases. The bleeding is usually capillary and, when visible, is in the nature of oozing from the gums, the nose, the uterus, the bowel and the kidney. Treatment consists of transfusion and splenectomy, neither of which is aimed at the true etiology. Transfusions are repeated during the acute stage and splenectomy is considered only when the disease becomes chronic. Irradiation with ultraviolet rays, in the author's opinion, is not of value. Green reported a case of thrombocytopenic purpura successfully treated by repeated transfusions and splenectomy.

Anschütz²⁶ observed that the prospects for cure by splenectomy in cases of chronic essential thrombopenia are satisfactory in the few cases studied, especially when the blood platelets remain high. Splenectomy in cases with low platelet counts also has given satisfactory results. The operative mortality ranges from 6 to 8 per cent in the chronic cases as compared with 70 to 80 per cent in the acute cases. The rapid course of the disease makes it imperative to choose the proper period of the disease for surgical intervention. The indications for surgical intervention depend on the duration and severity of the disease. The complications following splenectomy done in acute cases do not appear following operation done during the chronic stage.

[COMPILERS' NOTE.—Our knowledge of the dyscrasias associated with splenomegaly is increasing. The value of splenectomy in some of these conditions remains problematic. Giffin²⁷ stated, however, that in two diseases, namely, hemolytic jaundice and purpura hemorrhagica,

26. Anschütz, W.: Ueber Milzexstirpation bei Thrombopenien mit besonderer Berücksichtigung der akuten Fälle, *Beitr. z. klin. Chir.* **142**:1, 1928.

27. Giffin, H. Z.: Splenectomy, In: *Collected Papers of the Mayo Clinic*, Philadelphia, W. B. Saunders Company, 1927, vol. 19, pp. 637-644.

the results following splenectomy are so uniformly good that the indication for the operation depends almost entirely on a satisfactory diagnosis being made. W. J. Mayo²⁸ said that it is in the three blood dyscrasias, splenic anemia, hemolytic icterus and purpura hemorrhagica, that splenectomy is seen at its best.]

STOMACH

Duodenal and Gastric Ulcers.—Deaver²⁹ was of the opinion that operation is preferable to medical management in chronic ulcers of the duodenum and stomach. In bleeding duodenal ulcers, excision by knife or cautery, if possible, is advisable, and this should be followed with gastroduodenostomy or gastro-enterostomy. Deaver does not advocate subtotal gastrectomy for duodenal ulcer, unless, in the case of a bleeding ulcer, it is not possible to remove all of the periulcerous exudate with the ulcer. Subtotal gastrectomy, however, is indicated in gastric ulcer with very few exceptions. He favors the Billroth II type of resection.

Lewishon³⁰ said that duodenal ulcers and gastric ulcers are grouped collectively under the term gastroduodenal ulcers by many European surgeons because they believe that the etiologic factors are the same in both lesions. There are three surgical methods of treating ulcers: (1) local excision with or without gastro-enterostomy, a procedure which is often impossible because of an immobile duodenum or because of the site of the ulcer; (2) sleeve resection, which may or may not result in an hour-glass contraction of the stomach, and (3) partial or subtotal gastrectomy.

Lewishon stated that subtotal gastrectomy for both gastric and duodenal ulcer is the operation of choice because in this procedure the ulcers are entirely removed; the acid-bearing portion of the stomach is removed and the gastric acidity is greatly reduced thereby. He said that the mortality is low and the number of recurrences is less than after gastro-enterostomy.

[COMPILERS' NOTE.—Duodenal ulcer and gastric ulcer are separate and distinct lesions. Their etiology is not known. Duodenal ulcer occurs ten times as frequently as gastric ulcer. A duodenal ulcer almost never becomes malignant. Gastric ulcer may be malignant from the start, or it may become malignant. Duodenal ulcer is a combined medical and surgical problem. Every gastric ulcer is a surgical problem.

28. Mayo, W. J.: The Enlarged Spleen, In: Collected Papers of the Mayo Clinic, Philadelphia, W. B. Saunders Company, 1927, vol. 19, pp. 624-631.

29. Deaver, J. B.: Chronic Ulcer of Duodenum and Stomach, Surg. Gynec. Obst. 46:161, 1928.

30. Lewishon, Richard: Gastroduodenal Ulcers: Partial Gastrectomy Versus Gastro-Enterostomy in Their Surgical Treatment, J. A. M. A. 89:1649 (Nov. 12) 1927.

Whenever possible in duodenal ulcer, we excise the lesion, take out a section of the pyloric sphincter muscle and close it as in gastro-duodenostomy. All gastric ulcers should be excised. This is done either by local excision combined with gastro-enterostomy or by partial gastric resection. Occasionally a gastric ulcer is so situated that it cannot be excised.]

Hemorrhage from the Stomach and Duodenum.—Balfour³¹ said that massive hemorrhage in patients with duodenal and gastric ulcer rarely is fatal, and that repeated hemorrhages may or may not result in severe secondary anemia. Surgical treatment in acute, massive gastric hemorrhage is to be avoided because the mortality rate is higher than when patients are treated by medical means. Duodenal ulcer is the most common cause of hemorrhage from the stomach and duodenum. Of 1,072 patients operated on for duodenal ulcer, there was a history of gross hemorrhage in 184 (18 per cent). Blood was passed by bowel alone in 25 per cent, and was vomited alone in 27 per cent. Forty-eight per cent of patients gave a history of having vomited blood and passed it by rectum. Half of the patients had one hemorrhage only; the other half could recall two or more hemorrhages. The intervals between hemorrhages varied from one month to eighteen years. Patients with duodenitis may or may not give a history of hemorrhage. The causes of gastric and duodenal hemorrhage are not clear. Sometimes erosion of the gastroduodenal or superior pancreaticoduodenal artery seems to be the cause. In some cases gross defect cannot be found in the mucous membrane to account for the hemorrhage.

Mann, as a result of his experience in experimentally produced ulcers in dogs, was of the opinion that the hemorrhage may come from vascular buds in the granulation tissue which forms in the base of a healing ulcer or that actual mucous erosions are responsible. Such erosions often heal with great rapidity and do not leave a scar.

The treatment for duodenal ulcer associated with hemorrhage is surgical. The object is to relieve the patient of the symptoms of ulcer and to protect him against recurrence of the hemorrhage. Direct excision of the lesion, or cauterization, are the best methods of attack. Indirect operative procedures are of less value. Balfour stated that only 22 per cent of duodenal ulcers can be excised.

Balfour found that gastric ulcer is complicated by gross hemorrhage in 20 per cent of cases. Fatal hemorrhage from a gastric ulcer is rare. In bleeding gastric ulcers hematemesis occurred alone in 28 per cent, melena alone in 10 per cent, and both hematemesis and melena occurred in the same person in 62 per cent of cases. Gastric ulcers were surgi-

31. Balfour, D. C.: Management of Lesions of the Stomach and Duodenum Complicated by Hemorrhage, J. A. M. A. 89:1656 (Nov. 12) 1927.

cally accessible in 87 per cent of cases. In gastric carcinoma, gross hemorrhage occurred in only 7.5 per cent of cases. Microscopic hemorrhage, on the other hand, is common in cases of carcinoma.

Delore and de Girardier³² stated that the question of whether hemorrhage from gastric or duodenal ulcers belongs to the domain of the clinician or the surgeon is still a subject of debate. Cases of hemorrhage cannot be referred to as mild, moderate and severe, because alarming symptoms may arise in cases of profuse hemorrhage and yet the patient may make a rapid recovery provided hemorrhage does not recur. The difficulty and danger lie in recurrence of the bleeding. The source of the hemorrhage varies. It may come from the highly inflamed mucosa surrounding the ulcer or from erosions of smaller or larger vessels; the latter occurrence is more frequent than is generally thought. The prognosis in each case is therefore doubtful. The medical treatment consists of rest, lavage with hot water, injections of serum and blood transfusions. Why one patient may recover and another may not, under medical treatment, cannot be determined. Surgical treatment, therefore, is justified, although its seriousness is not to be minimized. If the patient comes under observation during the first hemorrhage, operation should be postponed until he has recovered from the immediate shock. If a patient comes under observation after repeated hemorrhage, the indication for operative procedure is further supported. Delore and de Girardier stated that the ideal procedure at operation is resection. Gastro-enterostomy should be limited to those cases with stenosis of the duodenum.

[COMPILERS' NOTE.—In both preoperative and postoperative bleeding from the stomach or duodenum, it is well to wait as long as possible before resorting to transfusion of blood. The sudden rise in blood pressure following transfusion frequently starts a fresh hemorrhage and may do more harm than good.]

Gastrojejunal Ulcers.—Wright³³ believed that gastrojejunal ulcers may occur after partial gastrectomy, rarely after pyloroplasty, and most often after gastro-enterostomy. He expressed the opinion that the cause of the primary ulcer is probably, also, the cause of the secondary ulcer. Gastric acidity is an important etiologic factor because the secondary ulcers form at the stoma where the acids have not yet been neutralized and because gastrojejunal ulceration occurs most commonly after gastro-enterostomy for duodenal ulcer which is accompanied by high acidity. Gastrojejunal ulcers occur less frequently following gastro-enterostomy in patients in whom the acids have been markedly

32. Delore, X., and de Girardier, J.: *Au sujet du traitement chirurgical des hémorragies gastro-duodénales d'origine ulcéreuse*, Presse méd. **36**:1092, 1928.

33. Wright, G.: *Gastro-Jejunal Ulceration*, Canad. J. M. & S. **63**:8, 1928

reduced by operation. The type of suture material used, and the use of clamps, are not of much significance in the etiology. Infection is a more significant factor, and Wright never does gastro-enterostomy in the presence of perforation, preferring merely to close the opening.

Gastrojejunal ulceration usually follows gastro-enterostomy, especially the Roux type of operation or gastro-enterostomy with entero-enterostomy. Fifty per cent of the secondary ulcerations are on the line of the anastomosis and encroach on both the stomach and the jejunum. Gastrocolic fistula, when present, usually follows posterior gastro-enterostomy. When secondary ulceration occurs after anterior gastro-enterostomy, it frequently presents itself in the anterior abdominal wall. Tenderness over the left rectus muscle, opposite or a little below the umbilicus, is an important physical sign. Roentgenographic examination may show irregularity of the stoma, and the stoma always is narrowed.

The methods of treatment have varied. The ulcer may be excised locally; the anastomosis may be excised together with the ulcer and a new anastomosis may be made; the anastomosis may be excised and the normal gastro-intestinal channel may be restored; finally partial gastrectomy may be done, which according to Wright is the operation of choice. When a jejunocolic or gastrocolic fistula is present, the organs must be separated and the opening in the colon must be closed, after which the other conditions are attended to. It is best to do a secondary operation before a colonic fistula develops.

Lewishon³⁰ reported 92 operations of gastro-enterostomy for ulcer of the duodenum at Mount Sinai Hospital in New York from 1915 to 1920. Of these, 47 per cent resulted in cure, 19 per cent of the patients still had slight complaints and 34 per cent developed gastrojejunal ulcers. Since November, 1922, all patients with duodenal and gastric ulcers at Mount Sinai Hospital have been treated by subtotal gastrectomy. Lewishon recommended this procedure without hesitation in all cases of gastric and duodenal ulcers.

[COMPILERS' NOTE.—The percentage of jejunal ulcers following gastro-enterostomy for duodenal ulcer is difficult to determine, but in our experience the frequency is about 3 per cent. Gastrojejunal ulceration occasionally follows partial gastrectomy for duodenal ulcer. We believe that most duodenal ulcers can be handled better by some less radical procedure than partial gastric resection. That absolutely sound principles have not been arrived at in the treatment for duodenal ulcer is shown by the different methods used in various clinics and is perhaps best exemplified by what has happened at Bier's clinic in Berlin. There change has been made from doing simple gastro-enterostomy in cases of duodenal ulcer to the radical method of resection, then back again to doing gastro-enterostomy, and at the present time a stand midway

between the two is taken. We prefer, if possible, to excise duodenal ulcers, but gastro-enterostomy has given excellent results in many cases, especially if there is pyloric obstruction.]

Starlinger³⁴ has shown by experiments on dogs that the mucosa of the descending portion of the duodenum has increased resistance against formation of ulcer. He does not believe that it is the neutralizing effect of bile and pancreatic secretion alone which prevents formation of ulcer in dogs after end-to-side gastroduodenostomy. In man, this operation may be considered as especially likely to prevent the formation of secondary ulcers. In this procedure, however, there is the possibility of obstruction by pressure from the superior mesenteric artery. Starlinger has tried to prevent this by a modification in technic. He mobilizes the duodenum from both sides, cuts the duodenum and reunites it by end-to-end anastomosis in front of the mesenteric artery, bringing the anastomosis through a new opening in the mesocolon near the middle colic artery. He stated that only time will determine whether this method of gastroduodenostomy modeled after the Billroth I method will be of value in the surgical management of cases of gastric and duodenal ulcer.

Wilkie² has recently been doing gastroduodenostomy after the manner of von Eiselsberg in cases of duodenal ulcer. He joins the anterior portion of the stomach near the pylorus to the second portion of the duodenum about opposite the ampulla of Vater. In this procedure, it is necessary to mobilize the second and third portions of the duodenum, which readily can be done by incising the peritoneum along the outer or convex border of the duodenum. Wilkie believed that this procedure offers all the advantages of gastrojejunostomy and practically eliminates the danger of the occurrence of a secondary or stomal ulcer, because the acid content of the stomach is emptied into the intestine near the same point that the alkaline secretions, bile and pancreatic juice enter the bowel.

Gastritis.—Konjetzny³⁵ was of the opinion that recent anatomic and clinical investigations have awakened new interest in the treatment for gastritis. He gave the following suggestions for detecting gastritis in its acute and chronic form at the time of operation. In acute gastritis, there is marked reddening of the serosa and more or less edema of the gastric wall which makes it seem plastic. The regional lymph

34. Starlinger, G.: *Versuche zur Säureresistenz und Geschwürsbereitschaft des infrapapillären Duodenums, sowie zum Ausbau der terminolateralen Gastroduodenostomie im Rahmen der ersten Methode Billroths*, Arch. f. klin. Chir. **149**: 593, 1928.

35. Konjetzny, G. E.: *Gibt es eine Anzeige zur chirurgischen Behandlung der Gastritis?* Arch. f. klin. Chir. **151**:370, 1928.

nodes are freshly enlarged and soft. There is slight edema of the gastric attachments of the mesogastrium and gastrocolic ligament.

Chronic gastritis, when associated with subacute inflammatory reactions, causes reddening of the serosa overlying the pyloric antrum. This corresponds to Schoemaker's "red stomach." There is more or less thickening of the gastric wall; the thickness increases from the antrum to the pylorus. This increased thickness of the gastric wall, as the pylorus is approached, is almost pathognomonic of chronic gastritis. There may be tumor-like thickening of the pylorus, often with pyloric obstruction which Konjetzny termed "stenosing gastritis." The thickening of the gastric wall may be nodular, a type which is called hyperplastic gastritis. Perigastritis usually is present on the posterior wall. There is chronic inflammatory enlargement of the lymph nodes along the greater and lesser curvature, most marked in the region of the antrum. Clinically, these two main types are often combined; the most marked evidence of inflammatory reaction is in the pyloric region.

The problem of gastritis is of clinical significance: first, because of the frequent recurrence of attacks of acute gastritis in cases with chronic inflammatory changes in the gastric mucosa; second, because epithelial proliferation in chronic gastritis generally is conceded to have precancerous proclivities.

Konjetzny discussed the indications for the surgical treatment in acute gastritis and presented three cases in which the clinical picture resembled that of perforated ulcer with peritoneal involvement. Severe hemorrhages may occur in gastric erosions which may develop in acute gastritis, and operation, in these instances, must depend on accurate determination of the source of the bleeding. A bleeding ulcer demands operation, but generalized bleeding from acute gastritis may tax the ingenuity of the surgeon as to whether surgical or medical management would give the best results. By gastrotomy, definite evidence may be gained of the source and nature of the bleeding. Jejunostomy has given good results when performed in cases of diffuse gastric hemorrhage. Konjetzny believed that medical treatment should be given in cases of simple acute ulcerative gastritis and that they should be considered of a surgical nature only if they fail to respond to medical management. Only those cases in which the gastritis is confined to the antrum pylori are amenable to surgical treatment. Generalized gastritis is not a surgical condition.

Pyloric stenosis and pylorospasm frequently are found associated with chronic gastritis. In most of the specimens of stomachs resected for chronic gastritis, thickening of the pyloric muscle is found. In hyperplastic chronic gastritis, or polypoid gastritis, there may be evidence of carcinomatous degeneration. Such precarcinomatous and carcinomatous areas may be present also in atrophic gastritis. The

polypoid form of gastritis usually can be diagnosed with the aid of the roentgen rays, but the diagnosis of atrophic gastritis can be made only by exclusion. In certain cases, gastroscopic examination has given the necessary evidence.

Konjetzny said that pyloroplasty has not been found satisfactory in the surgical management of acute or chronic gastritis, but has proved of value in cases of pylorospasm without definite evidence of gastritis. Polypoid gastritis presents a surgical indication for resection. The surgical indications in cases of simple atrophic gastritis are indefinite. Several cases in which resection has been performed showed beginning carcinomatous changes, and surgical intervention in this group remains an open question. Gastro-enterostomy has proved definitely harmful in cases of simple chronic gastritis.

[COMPILERS' NOTE.—Inflammatory lesions have a definite place in diseases of the stomach and duodenum. Duodenitis, either alone or in association with duodenal ulcer, is relatively common. Gastritis also occasionally occurs alone but usually is found in association with gastric or duodenal ulcer. We also have operated in several cases of supposed gastrojejunal ulceration and have found only well marked jejunitis and gastritis without true ulcer.]

Pylorospasm in Adults.—C. H. Mayo³⁶ said that it is probable that neither duodenal nor gastric ulcer occurs without accompanying pyloric spasm. Disease of the appendix and gallbladder tends to produce pyloric spasm. The pylorus and duodenum get their nerve supply from a large branch of the vagus that goes directly from the region of the cardia to the liver. For the last two years, in cases in which trouble in the stomach is due to reflex spasm of the pylorus, C. H. Mayo has divided the muscle of the pyloric ring at the upper border; in some cases also he has cut away the superior attachment of the first 2.5 cm. of the duodenum and the last 2.5 cm. of the pylorus in the hope of separating the branches of the vagus at this point. Because lesions at the angle of the stomach produce marked pylorospasm, C. H. Mayo recently has been dividing the tissues above the angle, cutting into the wall of the stomach so as to be sure of dividing the branches of the vagi. This slight additional procedure apparently has been of some benefit, but many further observations will have to be made before definite conclusions can be reached.

Hypertrophic Pyloric Stenosis in Infants.—Kirschner³⁷ reported 21 consecutive operations without mortality for pylorospasm in infants.

36. Mayo, C. H.: Division of the Vagi for Pylorospasm, *Ann. Surg.* **88**:669, 1928.

37. Kirschner: Die operative Behandlung des Pylorospasmus der Säuglinge, *Arch. f. klin. Chir.* **152**:509, 1928.

He used an incision in the median line and divided the pyloric muscle longitudinally with a knife. He emphasized that the muscle must be completely divided. The incision should extend a little onto the stomach and onto the duodenum. Kirschner considered the operation indicated when the infant has failed to improve after from five to eight days on medical management.

Kühl,³⁸ in discussing Kirschner's paper, pointed out that it is incorrect to give the impression that there is no risk in operating on infants for pylorospasm. He estimated the mortality rate at about 16 per cent.

Cardiospasm.—Keller,³⁹ in a case in which nonoperative dilatation of the cardia was unsuccessful, made an anastomosis between the fundus of the stomach and the lower end of the esophagus. The patient was cured. The operation is not offered as a substitute for nonoperative treatment of cardiospasm when done by an expert, but in view of the fact that the mortality following nonoperative dilatation in general hands is high, this operation, according to Keller, presents a method whereby the general surgeon may handle such cases.

[COMPILERS' NOTE.—In most cases, cardiac spasm can be cured by dilatation through the esophagus. A hydrostatic dilator is used and is guided into position by means of a silk thread which previously has been swallowed. Often a single dilatation is sufficient, but sometimes the procedure has to be repeated. We⁴⁰ recently were forced to operate on a patient in whom the hydrostatic dilator could not be introduced. In this case the stomach was opened and the cardiac opening was dilated manually from below.]

Gastric Ulcer and Carcinoma.—Scott⁴¹ was of the opinion that carcinoma does not develop from chronic gastric ulcer as often as is generally believed. He thought that many of the gastric ulcers in which there is coexisting carcinoma were primarily carcinomatous. Scott stated that there is no clinical method of distinguishing between a chronic gastric ulcer and early carcinoma with ulceration. All gastric ulcers, therefore, should be treated as though they were carcinomatous.

Walton⁴² was able to establish a definite relationship between gastric ulcer and carcinoma in 25 cases from a series of 228 cases of carcinoma of the stomach in which surgical treatment was employed.

38. Kühl, in discussion on Kirschner: Arch. f. klin. Chir. **152**:173, 1928.

39. Keller, W. L.: Operative Relief of Cardiospasm Where Dilatation Has Failed, Ann. Surg. **88**:58, 1928.

40. Nagel, G. W., and Judd, E. S.: Reports of Unusual Cases Observed in the Clinic of E. Starr Judd, S. Clin. N. Amer. **7**:1391, 1927.

41. Scott, W. J. M.: The Relationship of Carcinoma and Callous Gastric Ulcer, Surg. Gynec. Obst. **46**:199, 1928.

42. Walton, A. J.: Carcinoma of the Stomach, Lancet **2**:438, 1928.

[COMPILERS' NOTE.—Opinions differ as to the number of benign gastric ulcers which may become malignant. Moynihan⁴³ gave a figure as high as 21.8 per cent. Most German surgeons believe the association of malignant lesions and gastric ulcer an incidental occurrence rather than that one is secondary to the other. The significant point is that a certain number of gastric ulcers are malignant, whether they were malignant from inception or not, and gastric ulcer is, therefore, a surgical lesion.]

Carcinoma of the Stomach.—Balfour⁴⁴ advocated partial gastric resection in two stages for carcinoma of the pyloric end of the stomach with lymphatic involvement, with posterior fixation and with marked inflammatory reaction of the surrounding tissues. First, an anterior or posterior Polya type of operation, with or without entero-anastomosis, is done, and the pyloric end of the stomach is closed. In from ten to twelve days, when the condition of the patient is improved and the inflammation has had a chance to subside, the pyloric end of the stomach can be removed.

Walton⁴² reviewed the pessimism in the public mind regarding the fatal issue in carcinoma. This is especially true of carcinoma of the stomach because the early diagnosis is associated with much difficulty and the late prognosis is unsatisfactory. He presented a series of 229 cases of carcinoma of the stomach in which operations were done and 1,086 cases of simple chronic ulcers in which the patients, likewise, were subjected to operation during the same period, from 1913 to 1928. In this series there was one carcinoma of the stomach for every six gastric operations. Walton presented a chart showing that the cases with ulcer during this period have increased threefold, whereas the number of carcinomas has remained constant year by year. Duodenal ulcers are included in the chart and form the largest proportion of this series. Ulcers of the lesser curvature of the stomach also have increased threefold since 1913. To explain the relative increase of benign ulcer over carcinoma, Walton suggested that many patients have been saved from carcinoma by having ulcers treated surgically during the benign stage.

Since recurrences following operations for carcinoma of the stomach are found most frequently in the liver and deep lymph nodes, Walton was of the opinion that improvement in late results does not lie in more extensive operations. The fact that only about a third of the total number of patients with carcinoma are operated on when first seen led Walton to state that any persistent dyspepsia, occurring after the

43. Moynihan, B.: *Personal communication.*

44. Balfour, D. C.: A Method of Carrying Out Two-Stage Operations for Carcinoma of the Stomach, *J. A. M. A.* 90:1936 (June 16) 1928.

age of 40 years in a patient with a clear history, is to be regarded as due to carcinoma until the disease can be definitely eliminated.

Benign Gastric Neoplasms.—Balfour²¹ said that only 1 per cent of gastric neoplasms are benign. He classified 50 benign neoplasms of the stomach as follows: fibro-adenomatous polyps, 14; adenomas, 4; fibromas, myomas, fibromyomas, adenomyomas and myxofibromas, 23; hemangiomas, 4; polyposis, 4; hypertrophied mucosa, 2; papilloma, 1; dermoid cysts, 3, and hypertrophied pyloric muscle, 3.

Balfour stated that if a lesion can be shown to be present in the stomach, even in the absence of hemorrhage or marked symptoms, the treatment is surgical because it has been shown that 3 of 4 intragastric lesions are malignant (McVicar).

APPENDIX

Acute Appendicitis.—Eliason and Ferguson⁴⁵ have called attention to the fact that appendicitis has been little discussed since 1915. They found that the mortality from acute appendicitis has risen in the last twelve years. Statistics show that death occurs most frequently in those cases in which the diagnosis is delayed until the disease is not any longer confined to the appendix.

Eliason and Ferguson studied 675 cases which by laboratory reports and examination of gross specimens were proved to be cases of acute appendicitis. As soon as the diagnosis was made, operation was performed. Every patient was operated on in whom rigidity overshadowed distention, providing the vascular system was still competent. Low blood pressure associated with high temperature and cold extremities was a contraindication to operation. In cases of delayed operations, the incision was made under local anesthesia and a drain was placed in the pelvis; the appendix was not removed unless it presented in the wound. Drainage was necessary in at least one of every four cases, and was most often necessary in those patients who were less than 10 or more than 40 years of age.

From a diagnostic point of view, too much stress has been placed on tenderness over McBurney's point. Of 468 patients, only 44.7 per cent had tenderness in this region. Thirty-one per cent had rectal pain and tenderness. In 16.9 per cent of patients in whom the appendix was in the pelvis, pain was felt in the epigastrium. Rigidity was absent in 34.2 per cent of the cases in which the appendix lay to the left of the cecum and over the brim of the pelvis, and was most marked in cases in which the inflammation extended by contiguity to the abdominal wall.

45. Eliason, E. L., and Ferguson, L. K.: Mortality Factors in Acute Appendicitis, *Ann. Surg.* 88:65, 1928.

Nausea and vomiting, fever and leukocytosis are not constant reliable signs. In from 60 to 70 per cent of cases, one or more symptoms were atypical; in 18.6 per cent the leukocyte count was less than 10,000.

The mortality rate in the entire series was 5.5 per cent. In the cases in which drainage was not instituted, the mortality was 1.07 per cent. Approximately 50 per cent of the patients did not reach the surgeon until the third day, and 34 per cent did not reach the surgeon until the fourth day. The most frequent complications were peritonitis and intestinal obstruction; peritonitis was the greatest factor in the mortality.

[COMPILERS' NOTE.—The problem of acute appendicitis remains one of early diagnosis and operation. This depends on the confidence of the laity in the physician and the acumen of the physician, and is not likely to undergo any immediate radical change.]

Martens⁴⁶ stated that the mortality in patients with appendicitis associated with chills is double that of similar cases without chills. All patients with appendicitis who have chills should be operated on immediately. If twenty-four hours intervened between the first chill and the time the patient is operated on, it is advisable to ligate the ileocolic vein, especially if there is inflammatory infiltration of the mesocolon. It is best also to remove the entire meso-appendix. If pus is encountered in the meso-appendix, ligation of the ileocolic vein also is indicated. If chills develop after appendectomy for acute appendicitis, or if other symptoms of pyemia develop, Martens advised that the abdomen be reopened and the ileocolic vein ligated. If chills continue to recur after an operation for acute appendicitis, careful study of the blood picture, roentgenographic examination and punctures of the liver may reveal the presence of hepatic abscess. The timely drainage of such an abscess may prevent an otherwise fatal termination.

Deaver⁴⁷ believed that the appendix deserves first place as a focus of infection, not excepting the teeth, tonsils and sinuses. He stated that duodenal ulcer, gastric ulcer and cholecystitis, and abscesses of the liver are frequently due primarily to an infected appendix. Deaver was of the opinion that when a diagnosis of appendicitis has been made in the absence of general peritonitis, appendectomy should be done at once, because he believed that expectant treatment has resulted in many complications and deaths. He placed more stress on a high proportion of polymorphonuclear leukocytes in the differentiated blood smear than on a leukocyte count.

46. Martens, M.: Schüttelfröste und Blinddarmentzündung, München. med. Wchnschr. 75:335, 1928.

47. Deaver, J. B.: Appendicitis, J. A. M. A. 90:1679 (May 26) 1928.

Drainage for Appendicitis.—Weeden⁴⁸ advised the use of the Gibson-Mikulicz drain in operations for acute appendicitis. The drain consists of a square of rubber dam folded two or three times in the form of a cornucopia. The apex of this cornucopia, which forms the lowest point of the dam, is snipped off and 3.75 cm. above this, the edges of the cornucopia are cut out making a perforation of 1.25 cm. With the finger in the apex, the tampon is filled with strips of packing. When the drain is removed on the third or fourth day, a cavity about 10 cm. in diameter remains. This method affords a large amount of drainage.

Weeden reported a series of 1,588 appendectomies for acute appendicitis. In 728 (45.84 per cent), closure was without a drain and in 860 (54.16 per cent) drainage was instituted. The mortality rate in the cases in which drainage was instituted was 4.9 per cent, and in the cases in which drainage was omitted, 0.55 per cent. In Weeden's opinion, the drain is most valuable in those cases in which there is spreading peritonitis. Other advantages are that there is immediate lessening of toxemia, as shown by lowered temperature and pulse rate; the drain is easily removed and the wound is left open, therefore there is no secondary infiltration or infection of the abdominal wall; there is practically never any pocketing or formation of secondary abscesses and fecal fistulas develop in only a small number of cases (1.2 per cent); the adhesions produced, while firm enough to form a cavity for abscess, nevertheless do not give trouble and apparently disappear later. The disadvantages of the drain are that it increases the period of hospitalization; the average time, being 23.4 days as against from 17.1 to 18.6 days with other types of drains; hernia occurs in from 11.4 to 14 per cent of cases, and there is a possibility of evisceration, but this rarely occurs. Weeden believed that the advantages of the drain far outweigh its few disadvantages.

Traumatic Appendicitis.—McGeary⁴⁹ was of the opinion that the question of traumatism as a possible etiologic factor in appendicitis is of interest to the surgeon because of its medicolegal aspects. The dependent position of the appendix, its rather poor supply of blood and its bacteria-filled lumen are factors which must be considered in estimating injury to the appendix. McGeary presented data from five cases in which appendiceal symptoms and pathologic lesions in the appendix were present after traumatism of various forms. He said that if appendicitis is accepted to be the result of an accident or of trauma,

48. Weeden, W. M.: The Gibson-Mikulicz Drain in Acute Appendicitis: With Report of 1,588 Cases, *Ann. Surg.* **88**:76, 1928.

49. McGeary, W. C.: Traumatic Appendicitis, *Internat. J. Med. & Surg.* **41**:449, 1928.

there should be good corroborative evidence that there has been a more or less definite continuous train of symptoms from the date of the accident to the time of the appendiceal attack.

Appendicitis in Children.—Walton⁵⁰ said that chronic appendicitis in children under 14 years of age is rare and often is confused with a condition that really is acute. This is due to the fact that early symptoms often are overlooked or discounted in young children. A diagnosis of chronic appendicitis in adults usually means visceroptosis and operation should not be done. However, in children the diagnosis of chronic appendicitis often in reality means an acute condition, and immediate operation is indicated.

Chronic Appendicitis.—Smith⁵¹ expressed the opinion that in the disease known as chronic appendicitis the appendix may be implicated but often is not, and its removal frequently fails to relieve symptoms. He believed that in many cases the symptoms are due to kinking and obstruction of a mobile cecum by peritoneal bands. In cases in which the cecum is dilated and thin-walled, instead of trying to plicate or suspend it, he relieves the constriction by cutting the offending peritoneal band and covers the raw surface with a free omental graft. The cecum immediately resumes its normal tone, color, thickness and peristaltic activity. In a series of 420 cases diagnosed as cases of chronic appendicitis, Smith had only 202 cases in which he believed symptoms would be relieved by appendectomy alone. In the remaining 218 cases, it was necessary to deal with other pathologic conditions encountered; in 186 of these there were definite pericolic membranes which crippled cecal peristalsis and caused cecal block.

[COMPILERS' NOTE.—The diagnosis of chronic appendicitis probably is too frequently made. A definite history of previous acute attacks is significant in making a diagnosis. In cases of indefinite abdominal symptoms all other possible causes for distress must be investigated.]

Various Positions of the Appendix.—Wakeley and Gladstone⁵² analyzed 5,000 cases in which the position of the appendix was noted at operation, at necropsy and in the dissecting room. The postcecal and retrocolic positions of the appendix were those most commonly observed; the appendix was in one or the other of these positions in 64.3 per cent of cases. The pelvic or descending position occurred in 32.1 per cent of cases. Other positions of the appendix were less commonly seen.

50. Walton, A. J.: *Appendicitis in Children*, Lancet 1:445, 1928.

51. Smith, R.: *Chronic Appendicitis*, Ann. Surg. 88:678, 1928.

52. Wakeley, C. P. G., and Gladstone, R. J.: *The Relative Frequency of the Various Positions of the Vermiform Appendix*, Lancet 1:178, 1928.

COLON AND RECTUM

Carcinoma.—Rankin⁵³ emphasized the significance of adequate preparation before resection in carcinoma of the colon and rectum. This consists primarily of adequate cleansing of the gastro-intestinal tract, supportive and dietary measures, and the institution of drainage by colostomy, preliminary to subsequent resection. Rankin performed twenty-six anterior resections of the rectosigmoid and of the upper part of the rectum with only one death.

Rankin⁵⁴ reported the use of spinal anesthesia in carcinoma of the colon, with good results. Its advantages are complete relaxation during operation and the absence of postoperative pulmonary complications. Statistical studies of large groups of cases of carcinoma of the colon and rectum indicate that in a high percentage of cases there is freedom from recurrence for from three to five years or more.

Rankin and Broders⁵⁵ made a study of the factors which influence the prognosis in carcinoma of the rectum and they found that the grade of malignancy determined according to Broders' classification is of greatest significance. They found that the total of good results following operations for carcinoma of the rectum decreased in inverse proportion to the grade of malignancy, whereas the total of poor results increased in proportion to it.

Stoger⁵⁶ stated that most German surgeons favor resection in carcinoma of the rectum, with conservation of the sphincter if possible. Of 303 cases, Stoger was able to resect the growth and to save the sphincter in 76. The mortality in this group was 15.8 per cent; 44.8 per cent remained well for a period of five years or more; 8 patients were well more than ten years and 4 more than twenty years following operation. All had normal function of the rectal sphincter.

Kirschner⁵⁷ stated that the ideal surgical method for treating carcinoma of the rectum has not been determined. He believed that every case of carcinoma of the rectum should be approached by the abdominal sacral route. By opening the abdomen, metastasis, if present,

53. Rankin, F. W.: The Technique of Anterior Resection of the Rectosigmoid, *Surg. Gynec. Obst.* **46**:537, 1928.

54. Rankin, F. W.: Surgical Procedures in Carcinoma of the Large Bowel, *J. Michigan M. Soc.* **27**:465, 1928.

55. Rankin, F. W., and Broders, A. C.: Factors Influencing Prognosis in Carcinoma of the Rectum, *Surg. Gynec. Obst.* **46**:660, 1928.

56. Stoger, K.: Zur resektion des Rectumkarzinoms, *Deutsche Ztschr. f. Chir.* **112**:232, 1928.

57. Kirschner, M.: Alte und neue Vorschläge zur Ausrottung des Mastdarmkrebses, *Der Chir.* **1**:1, 1928.

can be found and dissection can be carried out under direct vision with less danger of hemorrhage and infection; also, the mortality is lower in this method. Although Kirschner formerly recommended removal of the sphincter in all cases, he now recommends saving it whenever possible. The results in these cases are satisfactory. He believes an abdominal anus is always preferable to a sacral anus.

Küttner⁵⁸ reviewed a series of 1,301 cases of carcinoma of the rectum. Sixty-three per cent occurred in men and 36.7 per cent in women. The growth was close to the anus in 0.3 per cent. The prognosis in this group was poor, as early metastasis to the inguinal lymph nodes takes place. Seven and three tenths and 11.5 per cent of tumors occurred, respectively, in the pars perinealis and in the ampulla of the rectum; in these the prognosis was good. Sixty and seven-tenths per cent occurred in the ampulla proper; in this group, the prognosis was not so favorable, as the condition usually was discovered late. Eleven per cent occurred near the flexure; most of these cases are inoperable. Küttner recommended saving the sphincter whenever possible. He makes a sacral anus, as a rule, and uses the combined abdominal sacral operation only occasionally; he stated that it must first be shown that the mortality in this method is no greater and that the results are better. He reported 480 radical operations with 108 deaths, a mortality of 22.5 per cent.

In a group of 150 cases in which operation was done in the last seven years, the mortality was 16.4 per cent. Thirteen patients were operated on by the abdominal sacral route, and in this series there were 7 amputations of the rectum, with 2 deaths, a mortality of 29.5 per cent, and 6 resections with 4 deaths, a mortality of 66.6 per cent. The results following radical operation on the patients who survived operation were: patients living three years or longer, 46.5 per cent; more than five years, 32 per cent; more than eight years, 24.1 per cent, and more than ten years, 19 per cent. Of those patients who underwent palliative colostomy, 70 per cent died within the first year, 6 per cent lived three years and 2 per cent lived five years.

[COMPILERS' NOTE.—Surgical procedures in carcinoma of the colon are accompanied by a relatively high risk because of the presence of infection and because of the relatively poor supply of blood to the colon. Delayed healing following operation is due not to an actual paucity of blood supply to the colon, but to a lack of adequate anastomosing vessels. Preoperative preparation of patients is important. In cleaning out the gastro-intestinal tract, however, care must

58. Küttner, Hermann: *Der Mastdarmkrebs und seine chirurgische Behandlung*, Med. Klin. 25:4, 1929.

be taken not to lower the patient's resistance by too prolonged rest in bed, by catharsis or by insufficient diet.]

Blood Supply of the Colon.—Fischer⁵⁹ described two types of small arteries that are given off from the vessel that runs longitudinally in the mesentery, close to the attachment of the bowel. The smaller vessels supply that portion of the bowel which is near its mesenteric attachment. The larger vessels encircle the bowel and supply blood to the portion opposite the mesenteric attachment. These larger vessels pass through the bases of the appendices epiploicae. When the colon is fully distended, the vessels lie flush with the surface of the bowel, but when the intestine is collapsed they form a loop extending some little distance into the appendixes. In tying off the appendixes, these vessels are likely to be injured, thus interfering with the blood supply on the contramesial side of the bowel. Fischer recommended end-to-end anastomosis of the colon, but said that the bowel should be cut through diagonally and that care should be taken not to injure the vessels already described.

Colostomy.—Demel⁶⁰ devised an artificial abdominal anus which allows the patient to control bowel movement directly. The method consists in bringing out a portion of the bowel and surrounding it with a cylinder of skin. By a special mechanical device the patient can keep this part of the bowel clamped off and thus prevent the passage of content of the bowel through the distally placed opening. Demel performed the operation on six patients with good results. Closure of the bowel is well tolerated up to twelve hours.

[COMPILERS' NOTE.—Many methods have been devised for making a colostomy which will enable the patient to control the movements of the bowel. In our experience, complicated operations are unnecessary, and properly done colostomy, with the bowel brought out through a muscle-splitting incision on the left side, gives the best results. Lavage once daily, and simple dietary measures, are adequate to enable the patient to live in comfort and to attend to his work and pleasures in the normal manner.]

Diverticulitis of the Colon.—Monsarrat⁶¹ recommended conservative treatment rather than operation in acute diverticulitis of the colon, except in cases that have progressed to formation of abscess. Uncompli-

59. Fischer, A. W.: Inwieweit ist durch die Ablösung des Dickdarmfettheanges die Sicherheit der Dickdarmaht gefährdet, Arch. f. klin. Chir. **152**:638, 1928.

60. Demel, Rudolf: Eine einfache Herstellung des verschlussfähigen Kunstafters, Deutsche Ztschr. f. Chir. **110**:336, 1928.

61. Monsarrat, K. W.: Remarks on Surgical Treatment of Diverticulitis, Brit. M. J. **2**:41, 1928.

cated cases of chronic diverticulitis, the more common form of the disease, also are best treated medically. If a patient with chronic diverticulitis is operated on, Monsarrat advised that the bowel be wrapped in omentum to prevent the formation of a fistula of the bladder.

[COMPILERS' NOTE.—A temporary colostomy by which the content of the bowel is shunted to the outside frequently is of value in diverticulitis, especially if the disease is fairly well localized. Often, after a few months, during which the lower segment of bowel is irrigated daily, the lesion has healed sufficiently to allow closure of the colostomy opening. Occasionally the lesion may be resected.]

Syphilis of the Colon.—Chastenet ⁶² reported two cases in which abscesses of the colon, adherent to the abdominal wall, one of which had a fecal fistula, apparently were of syphilitic origin.

Infectious Granuloma of the Colon.—Mock ⁶³ reported three cases of infectious granuloma of the intestines. Such tumors appear to be due to excess reparative processes following low-grade infection and necrosis. The growths often reach an appreciable size and are readily mistaken for malignant tumors.

Obstruction of the Colon.—Haggard ⁶⁴ stated that operations for acute intestinal obstruction are accompanied by a higher mortality than generally is supposed. The causes for this are the promiscuous use of purgatives, failure to recognize the conditions early and delay of operation. Haggard described enterostomy as a surgical method of treating intestinal obstruction. He called attention to the disturbances in chemistry of the blood and recommended the intravenous administration of solutions of dextrose and sodium chloride.

Rosenstein and Köhler ⁶⁵ studied the question of the control of intestinal peristalsis in animals and showed that the injection of nicotine into the celiac ganglion caused marked increase in peristalsis in normal animals as well as in those with peritonitis. Nicotine paralyzed the synapsis between the preganglionic and postganglionic fibers of the autonomic nervous system. By injecting nicotine directly into the celiac ganglion, the action controlled by the splanchnic nerves is diminished.

62. Chastenet, de Gery: Deux cas de sigmoïdite suppurée avec infiltration de la paroi abdominale chez des syphilitiques, Bull. et mém. Soc. Nat. de Chir. **54**: 834, 1928.

63. Mock, H. E.: Infective Granuloma of the Intestines, Internat. J. Med. & Surg. **41**:1, 1928.

64. Haggard, W. D.: Acute Intestinal Obstruction, J. A. M. A. **90**:1424 (May 15) 1928.

65. Rosenstein, Paul, and Köhler, Hans: Ueber die Beeinflussung der Darm-paralyse durch Nikotininjektion in das Ganglion coeliacum, Deutsche Ztschr. f. Chir. **210**:315, 1928.

As these nerves are the antagonists of the vagi or motor nerves of the bowel, the action controlled by the latter is thereby increased. This action occurs even though the vagus is injured by toxins. The vagus is not affected by injection of the celiac ganglion, as synapsis between its preganglionic and postganglionic fibers does not occur at this point.

Following a careful study of the action of nicotine in animals, its therapeutic value was tested in human beings. The dosage used was from 5 to 8 mg. of fresh nicotine in 50 cc. of sterile water. The action of the drug appeared to take place only locally; there was no general reaction as a result of absorption of the nicotine. The 26 patients in whom it was tried all had marked paralytic ileus, mostly as a result of peritonitis, and all other methods used to relieve the ileus had failed. Rosenstein and Köhler believed that the most significant factor in causing death in ileus is the absorption of toxic products from the content of the intestine; therefore, elimination of this content is indicated. The paralysis of the bowel was overcome in 17 of the 26 patients; 9 of them subsequently died. One patient had multiple abscesses in the abdominal cavity; 2 had bronchial pneumonia; 1 died of cardiac failure; 2 died of sepsis following abortion, and 3 died as a result of the progress of carcinoma. Eight of the patients recovered.

The technic of injection is that used by Kappis and Finsterer in their method of splanchnic anesthesia; the approach is from behind, with the patient preferably in a sitting position. The method never must be used in mechanical ileus, as to use it would only make the condition worse. Rosenstein and Köhler were of the opinion that this method is a step forward in the treatment for paralytic ileus.

Ochsner, Gage and Cutting⁶⁶ induced splanchnic anesthesia in dogs with 1 per cent solution of procaine hydrochloride and found that it relieved ileus and produced peristalsis. They recommend splanchnic anesthesia in paralytic and adynamic ileus, and in mechanical ileus after the obstruction has been relieved.

PERITONITIS

Salzer⁶⁷ traced the etiology of the majority of cases of diplococcal peritonitis to infection from the genitalia. The differential diagnosis from appendicitis is possible but is necessary only in young girls. In boys there is always preceding diplococcal appendicitis which requires

66. Ochsner, Alton; Gage, I. M., and Cutting, R. A.: Treatment of Ileus by Splanchnic Anesthesia: Preliminary Report of Experimental Study, *J. A. M. A.* 90:1847 (June 9) 1928.

67. Salzer, Hans: Die Diplokokkenperitonitis beim Kinder, *Deutsche Ztschr. f. Chir.* 208:226, 1928.

immediate operation. Girls should be treated expectantly until the presence of pus in the abdominal cavity becomes a possibility, then operation is indicated.

David⁶⁸ showed that *Bacillus coli* was taken directly into the blood stream, as well as into the lymphatics, from the peritoneum of a normal dog. He also showed that the presence of a plastic exudate produced by intraperitoneal injection of emulsion of turpentine greatly hindered or prevented the passage of bacteria into the lymph or blood stream, whereas the presence of hypertonic solution of dextrose in the peritoneal cavity increased the rate of absorption of bacteria.

David and Sparks⁶⁹ found in an experimental study that diphtheria toxin, when injected into the normal peritoneal cavity of a dog, passed directly into the blood stream, as well as into the lymphatics, in sufficient quantities to prove fatal to guinea-pigs. In the presence of well developed plastic peritonitis, there was practically no passage of diphtheria toxin into the chyle, and it passed into the blood stream in much smaller quantities than from the normal peritoneum. The presence of hypertonic solution of dextrose in the peritoneal cavity of dogs increased the rate of absorption of diphtheria toxin by the blood stream and by the lymphatics.

David and Sparks concluded that the formation of a plastic exudate was to be regarded as a favorable process in peritonitis. Although they do not wish to press the analogy between the peritoneum of the dog and of the human being, they believed from their experiments that in the early hours of peritonitis the absorption of toxins and bacteria from the circulation directly and by way of the lymphatics is the dominant factor of danger; later, absorption from the peritoneum becomes less significant and local conditions, such as paralytic ileus, gain the ascendancy.

Brown⁷⁰ found in experimental studies on cats and dogs, in which peritoneal absorption is much like that in man, that absorption by way of the thoracic duct from the peritoneal cavity is a slow and unimportant process. He also found that the omentum plays little, if any, part in actual lymphatic absorption from the peritoneal cavity. Brown concluded that lymphaticostomy cannot be recommended as a procedure offering any hope to patients suffering from acute peritonitis.

68. David, V. C.: Peritonitis: An Experimental Study, Surg. Gynec. Obst. **45**:287, 1927.

69. David, V. C., and Sparks, J. L.: The Peritoneum as Related to Peritonitis, Ann. Surg. **88**:672, 1928.

70. Brown, K. P.: Peritoneal Lymphatic Absorption: An Experimental Investigation to Determine the Value of Lymphaticostomy, Brit. J. Surg. **15**:538, 1927-1928.

INTRA-ABDOMINAL HEMORRHAGE

Büttner⁷¹ attempted to answer the question of whether there is any worth while method of utilizing the blood found in the abdominal cavity in patients with severe intra-abdominal hemorrhage and turning it to a useful purpose. These patients suffer from the effects of diminished blood volume and accompanying deficiency in the oxygenating properties of blood; the first requirement is to supply these deficiencies. The most satisfactory method of accomplishing this is direct transfusion of properly grouped blood. Büttner suggested, as a matter of expediency, and because grouping would not be necessary, the possibility of reinfusing the functionally active free blood found in the abdominal cavity. There is also the danger of leaving large quantities of blood in the abdominal cavity for absorption by the peritoneum. The irritated peritoneum may be protected by evacuating any extravasated blood from the abdominal cavity.

THROMBOSIS AND EMBOLISM

Borchard⁷² stated that it is generally believed that thrombosis and embolism are on the increase but whether or not this is true is difficult to determine accurately. Thrombosis, embolism and infarcts must be considered together, and particular attention must be paid to the origin. Thrombosis of the saphenous vein often is incorrectly said to be the origin of a pulmonary embolus. Borchard saw a pulmonary infarct, and later thrombosis of the saphenous vein. The three factors in the causation of thrombosis are slowing of the blood stream, changes in the wall of the vessel and changes in the blood. He believed the condition of the blood to be the chief factor.

It is known that certain conditions predispose to thrombosis and embolism, namely, myoma, prostatic disease and carcinoma, especially carcinoma of the intestinal tract. On the other hand, operations on the thyroid gland are seldom followed by thrombosis and embolism. Infection increases the danger by two-thirds, especially if the infectious focus cannot be removed. Infections must also be considered which may have occurred several weeks previously, as, for example, influenza and angina. Slowing of the blood stream is significant in the first postoperative days, as the patient lies more quietly and breathes less deeply during this time. A great deal more statistical and experimental work must be done in order to clarify the ideas regarding the exact rôle of these causative factors. Treatment must be instituted largely on an empiric

71. Büttner, Georg: Zur Therapie schwerer Blutungen in die Bauchhöhle, Arch. f. klin. Chir. 150:93, 1928.

72. Borchard, A.: Ueber Thrombose und Embolie, Beitr. z. klin. Chir. 144: 163, 1928.

basis. Particular attention must be paid to the patient's heart, lungs and general constitution. Age, the possible presence of endocrine disturbances and the coagulation time of the blood also must be considered.

Certain conclusions can be drawn as to the possibility of a patient developing thrombosis and embolism. Special attention should be paid to preoperative preparation. Following operation active and passive movements should be begun as early as possible. Peripheral emboli are not so much feared as formerly, as embolectomy is followed by good results. Embolus must not be considered by the surgeon as an act of fate; somewhere there must have been something which could have been foreseen or prevented.

Tempsky⁷³ made a statistical study of thrombosis and embolism. Only pulmonary emboli which were proved to be present at necropsy are included in the following table.

Occurrence of Emboli

	Carcinoma of the Stomach			Pulmonary Embolus	
	Cases	Thrombosis	Per Cent		Per Cent
Total.....	1,458	45	3.8	12	0.8
Resection.....	496	17	3.4	5	1.2
Gastro-enterostomy.....	392	13	3.3	2	0.5
Exploration.....	467	12	2.5	3	0.6
Carcinoma of the Rectum					
Total.....	506	27	5.3	17	3.3
Preternatural anus.....	202	4	1.9	2	0.9
Amputation and resection...	304	23	7.5	15	4.9
Appendicitis					
Total.....	1,767	29	1.6	4	0.2
Chronic.....	819	5	0.5		
Acute.....	458	7	1.5		
Perforated.....	490	14	2.8	4	0.8

In cases of carcinoma of the stomach, thrombosis occurred more frequently in the saphenous and femoral veins of the right side than in those of the left side. Thrombosis was never diagnosed clinically in patients of this group who died of pulmonary embolism. In the cases following appendectomy, thrombosis could not be demonstrated clinically. In one case following operation for carcinoma of the rectum, there was thrombosis of the right saphenous vein on the eighth day, and on the sixteenth day the patient died of pulmonary embolus. In appendicitis, thrombophlebitis occurred much more commonly in cases with infection, and fatal pulmonary emboli occurred only in cases with infection. Thrombosis of the extremities in this group was greater than in previous groups, and it occurred twice as often on the left side as on the right. In carcinoma of the stomach and rectum, infection does not appear to play a great rôle as a causative agent. Intravenous treat-

73. Von Tempsky, Arthur: *Die Lungenembolie nach chirurgischen Eingriffen*, Beitr. z. klin. Chir. **144**:170, 1928.

ment is not a cause. Cachexia and extreme amounts of fat seem to be factors in death of patients from pulmonary embolism.

Nyström⁷⁴ stated that in Sweden 5 persons have recently been operated on, after the manner of Trendelenburg, for the removal of pulmonary emboli. Three patients were operated on by Nyström, with 1 recovery and 2 deaths. The other 2 patients, operated on elsewhere, recovered. In Nyström's patient who recovered, the circulation was stopped for one hundred and four seconds while the clot was removed by means of a suction apparatus. Studies made of this patient two months after operation showed the heart and the large vessels to be anatomically and functionally normal.

Meyer⁷⁵ reported that he had seen 7 pulmonary emboli in a series of 2,182 operations in one year. Six of the patients died so suddenly that operation for emboli was not possible. In a seventh case, the operation was performed but the patient died of pneumothorax produced through a fault in technic. In another case of pulmonary embolism the operation was successful.

Giertz⁷⁶ reported from his clinic in the last six years that there were 7,824 operations and 239 cases of thrombosis or embolism. Of the cases of embolism, 27 were pulmonary and operation was done in 4 cases. Two of these patients recovered. In none of the 4 operations was any anesthetic necessary; the patient was moribund at the time of operation.

Friedel⁷⁷ reported that at the Rudolfs-Spital in Vienna occasion has arisen for doing the Trendelenburg operation 6 times. None of the patients recovered. Friedel pointed out that diagnosis is not always easy. In 2 patients who died, apparently from pulmonary embolism, necropsy revealed that death had been from cardiac causes.

Stegemann⁷⁸ examined Kirschner's patient, the first patient successfully operated on for pulmonary embolism, four years after the operation and found her normal in every way.

DeCourcy⁷⁹ stated that fully 50 per cent of the serious pulmonary complications which occur after abdominal operations are the result of embolism. Advanced age of the patient and incision through the

74. Nyström, Gunnar: Erfahrungen in drei nach Trendelenburg operierten Fällen von Lungenembolie, *Arch. f. klin. Chir.* **152**:450, 1928.

75. Meyer, A. W., in discussion on Nyström: *Arch. f. klin. Chir.* **152**:97, 1928.

76. Giertz, in discussion on Nyström: *Arch. f. klin. Chir.* **152**:98, 1928.

77. Friedel, Robert, in discussion on Nyström: *Arch. f. klin. Chir.* **152**:100, 1928.

78. Stegemann, in discussion on Nyström: *Arch. f. klin. Chir.* **152**:101, 1928.

79. DeCourcy, J. L.: Postoperative Embolism, Venous Stasis and Its Prevention by Proper Posture After Lower Abdominal Operations, *Internat. J. Med. & Surg.* **41**:179, 1928.

anterior abdominal wall are two outstanding predisposing factors in postoperative pulmonary embolism. Sepsis appears to be only a contributing factor. Rough handling of tissues, endocrine disturbances with lowered metabolism and venous stasis may be considered as other causes in the development of postoperative pulmonary embolism. The use of Fowler's position, the pillow beneath the knees after gynecologic operations and restriction of movement tend to favor massive thrombosis by retarding venous circulation. DeCourcy advocated the reverse Fowler position after surgically clean operations in the lower part of the abdomen. This position consists of elevating the foot of the bed about 15 cm. and inserting a small, fixed pillow under the small of the back.

[COMPILERS' NOTE.—Pulmonary embolus continues to be one of the most dreaded postoperative complications. Fatal pulmonary embolus fortunately is rare. Many postoperative pulmonary complications undoubtedly are embolic in origin. In our experience, fatal pulmonary embolus occurs too rapidly to consider the question of surgical intervention. The patient who survives the immediate shock often recovers under expectant treatment. The diagnosis of pulmonary embolism, while usually plain, is not always so and may be confused with certain cases of cardiac failure.]

ANESTHESIA

Wymer⁸⁰ described Ombredanne's method of ether anesthesia. A rebreathing apparatus is used in which the exhaled carbon dioxide and ether pass directly into a bag and are reinhaled. The amount of ether used can be determined accurately and is considerably less than that used in the drop method. In one case, 450 Gm. of ether was required by the open method; in a case of the same type only 150 Gm. was required by Ombredanne's method. This lessening of the amount of ether required results in an appreciable decrease in postoperative pulmonary complications.

Melzner⁸¹ reviewed the subject of rectal anesthesia and gave his experience with tribromethanol (avertin). The manufacturers of this drug claim that it does not cause local irritation, that it does not produce unpleasant symptoms and that it is harmless and easily removed. Melzner has used the drug in 100 cases. The dosage used was 0.15 Gm. for each kilogram of body weight given as a 2.5 per cent solution in physiologic solution of sodium chloride. Morphine was given previous to injection. There was no local irritation. Light sleep was produced in from two to five minutes, and deep sleep in from ten to twenty

80. Wymer, I.: *Die aethernarkose nach Ombredanne*, Deutsche Ztschr. f. Chir. **212**:79, 1928.

81. Melzner, Ernst: *Zur Beurteilung der Rectalnarkose mit E. 107 (Avertin)*, Arch. f. klin. Chir. **148**:698, 1927.

minutes following injection. Sleep occasionally lasted ten hours and longer, with no postoperative vomiting. It produced unpleasant mental disturbances in some instances. In one patient, hallucinations lasted twenty-four hours. Complete anesthesia was produced in only 54 per cent of cases and in three cases there was complete failure. Following the administration of the drug, there is an increase in the pulse rate and a fall in blood pressure; the latter, in some instances, is alarming. There were four deaths. Two occurred during anesthesia; one of these patients had a tumor of the brain; the other had a carcinoma of the stomach for which palliative gastro-enterostomy was done. One patient with exophthalmic goiter died six hours following operation and another who had undergone excision of simple goiter, died twenty-four hours postoperatively. In this case, epithelial necrosis in both kidneys was found at necropsy. Melzner advised against the use of this drug.

Martin⁸² was able to produce complete narcosis in 96 per cent of cases by combining scopolamine and a proprietary double salt of morphine and narcotin with tribromethanol. The duration of full narcosis was from one and a half to two hours. The normal dosage is scopolamine, 0.00025 Gm.; proprietary double salt of morphine and narcotin, 0.03 Gm., and tribromethanol, from 0.13 to 0.15 Gm., for each kilogram of body weight. These dosages are varied slightly according to the age, weight and condition of the patient. Martin's series includes 104 cases of laparotomy.

Butzengeiger⁸³ has used tribromethanol in approximately 300 operations, including 200 of laparotomy, and believes that it has some distinct advantages over other forms of anesthesia. It can be given to the patient in bed, and sleep follows naturally; thereby the fear that many patients have of other forms of anesthesia is overcome. Butzengeiger did not have any fatalities. He stated, however, that at present only small doses must be tried and that complete anesthesia is not to be expected in every case.

Nordmann⁸⁴ has had favorable results with tribromethanol in 250 cases and believes that it is a step in advance in methods of anesthesia, although it is too soon to draw definite conclusions.

Sauerbruch⁸⁵ reported three cases in which tribromethanol produced ulceration of the large bowel which resulted in death; he warned against its widespread use until further careful investigation has been carried out.

82. Martin, B.: Vollnarkosen mit Avertin, *Arch. f. klin. Chir.* **152**:670, 1928.

83. Butzengeiger: Die Rectalnarkose mit E. 107, *Arch. f. klin. Chir.* **148**:95, 1927.

84. Nordmann, in discussion on Butzengeiger: *Arch. f. klin. Chir.* **148**:97, 1927.

85. Sauerbruch, in discussion on Butzengeiger: *Arch. f. klin. Chir.* **148**:99, 1927.

Reischauer⁸⁶ reported the case of a patient who died as a result of anesthesia with tribromethanol. Necropsy revealed marked fatty changes in the liver and kidneys.

Kirschner⁸⁷ pointed out that any new method of anesthesia must fulfil certain requirements; namely, that in all cases sufficient anesthesia must be produced and that this must be achieved without any greater risk than that which accompanies the methods of inhalation anesthesia now employed. Neither of these requirements has been fulfilled by tribromethanol up to the present time.

[COMPILERS' NOTE.—Rectal anesthesia with tribromethanol has been widely used in Germany. In a number of clinics it has been found useful and apparently in these clinics bad results have not been experienced from it. However, in an equal number, notably the clinic in Jena, Küttner's clinic in Breslau and Clairmont's clinic in Zurich, the drug is not used any longer because the physicians of these clinics believe it dangerous.]

86. Reischauer, in discussion on Butzengeiger: *Arch. f. klin. Chir.* **148**:100, 1927.

87. Kirschner, in discussion on Butzengeiger: *Arch. f. klin. Chir.* **148**:108, 1927.

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AIR EMBOLISM FROM THE PULMONARY VEIN

A CLINICAL AND EXPERIMENTAL STUDY *

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Air embolism, with the pulmonary vein as the portal of entry, may complicate nearly any surgical procedure on the lung. Graham¹ experienced two fatalities from this source in forty-five operations of cautery pneumectomy, and it has occurred in as simple a procedure as irrigation of an empyema cavity. Brauer² termed the condition arterial air embolism and emphasized its frequency as a complication of artificial pneumothorax. While the cause of the syncope, collapse and death that are occasionally seen during pneumothorax induction is not always clear, it is doubtless often air embolism. Stivelman³ reported seven instances occurring in 162 primary punctures; Forlanini⁴ had twelve in 134, and Sachs⁵ collected twenty-two in 1,122 from the literature.

Sharp distinction must be made at once between this form of air embolism and that in which air enters a peripheral vein, as the jugular or subclavian. In the former, air enters the peripheral arteries and may involve every organ and tissue, while in the latter air passes into the pulmonary arteries and exerts its effects on the lesser circulation and right side of the heart.

In this article are presented certain clinical and experimental data and deductions concerning air embolism from the pulmonary vein. A brief summary of current knowledge is given to introduce each phase

* Submitted for publication, May 13, 1929.

1. Graham, E. A.: *Ann. Surg.* **86**:174, 1927.

2. Brauer, L. D.: *Ztschr. f. Nervenhe.* **45**:276, 1912. Brauer, L.; Schröder, G., and Blumenfeld, F.: *Handbuch der Tuberkulose*, ed. 3, Leipzig, J. A. Barth, 1923, vol. 2, p. 461.

3. Stivelman, B. P.: *Am. J. M. Sc.* **165**:836, 1923.

4. Forlanini, C.: *Ergebn. d. inn. Med. u. Kinderh.* **9**:621, 1912.

5. Sachs, T. B.: *Artificial Pneumothorax in the Treatment of Pulmonary Tuberculosis*, J. A. M. A. **65**:1861 (Nov. 27) 1915.

of the subject. Complete reviews of the literature are available elsewhere.⁶

ETIOLOGY

Air may enter the pulmonary vein spontaneously or may be injected.

The venous pressure in the pulmonary circulation is ordinarily less than that of the atmosphere, and should the lumen of a vein be freely opened air is drawn into the blood stream. This has occurred in such operations as pneumectomy, pneumotomy, pulmonary decortication, dissection or probing within the lung and separation of the pleural adhesions. Injection of air or other gases directly or indirectly into the circulation has occurred in the production of artificial pneumothorax. The needle may accidentally enter the lung and one of its vessels, or when the puncture has been accurate and the gas enters the pleural cavity an adhesion between the lung and the wall of the chest may tear and open a pulmonary vein. Air from the pleural cavity may then enter the torn vessel.

Essentially the same type of embolism has been known to arise in other ways: Air that has entered a peripheral vein and has been carried to the right side of the heart occasionally finds its way through a patent foramen ovale into the left auricle.⁷ That the foramen ovale is frequently patent without evidence during life is well known. Herxheimer⁸ found from 20 to 50 per cent patent during routine examination at autopsy; Otto⁹ noted 286 in 1,130 consecutive autopsies in Dresden material, of which 200 admitted a probe only and eighty-six were of comparatively large size; Lubarsch¹⁰ found patency in 25 per cent, and Kaufmann¹¹ in 32.5 per cent.

In 1808, Bichat¹² demonstrated that when air is blown into the lungs of a living animal at a pressure no greater than the maximum expiratory effort of which the animal is capable, provided the pressure is maintained, air will leave the alveoli and enter the pulmonary capillaries. Enough air may thus be forced into the circulation to cause death, and the effect is, of course, the same as though the air had directly entered a pulmonary vein. Ewald and Kobert,¹³ in a painstaking study,

6. Schlaepfer, K.: *Bull. Johns Hopkins Hosp.* **33**:321, 1922. Wever, E.: *Beitr. z. Klin. d. Tuberk.* **31**:159, 1914.

7. Walcher, K.: *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **39**:314, 1926. Steindl, H.: *Wien. klin. Wchnschr.* **37**:206, 1924.

8. Herxheimer, quoted from Infeld, M.: *Wien. klin. Wchnschr.* **27**:1407, 1914.

9. Otto, W., quoted from Geipel: *München. med. Wchnschr.* **59**:1683, 1912.

10. Lubarsch and Ostertag, quoted from Steindl, H.: *Wien. klin. Wchnschr.* **37**:206, 1924.

11. Kaufmann, quoted from Steindl, H.: *Wien. klin. Wchnschr.* **37**:206, 1924.

12. Bichat, quoted from Beneke, R.: *Verhandl. d. deutsch. path. Gesellsch.* **16**:263, 1913.

13. Ewald, J., and Kobert, R.: *Arch. f. d. ges. Physiol.* **31**:160, 1883.

"Ist die Lunge luftdicht?," showed that this phenomenon is not one of alveolar rupture but of escape of air through normal stomas in the alveolar walls when a certain degree of distention is reached. On this principle has been explained the finding of air occasionally in the cavity of the left side of the heart of persons drowned¹⁴ or hanged¹⁵ and of infants who have received strenuous resuscitative measures.¹⁶ Neubürger¹⁷ suggested that the convulsions which sometimes occur in whooping cough are from cerebral embolism, air being forced into the blood stream from the alveoli during a paroxysm of coughing. At autopsy in these cases confirmatory evidence is found in the lesions of the brain.¹⁸

CLINICAL CASES

CASE 1.—A man, aged 42, had an illness of sixteen months' duration. The onset was insidious, with cough, fever, night sweats and progressive loss of weight. The sputum was abundant and fetid, and was constantly negative for tubercle bacilli. The diagnosis was bronchiectasis of the left lung and chronic empyema.

He was admitted to University of Iowa Hospital surgical service. A small empyema pocket in the left side of the chest was drained by rib resection. Some time later, by roentgen examination, a cavity was found in the left lung, and surgical drainage of the cavity was undertaken. With the patient under ethylene anesthesia, a piece of rib was removed at the posterior axillary line over the cavity. The pleural surfaces were found adherent, and an exploring needle, attached to a syringe, was passed into the lung. The resistance offered to the needle by the parenchyma of the lung was increased. At some points air was aspirated freely, at others blood. No pus was found and after a few punctures the attempt was abandoned. As the wound was being closed, the patient suddenly ceased to breathe and heart action could not be detected.

At autopsy, about one hour after death, air was found in large quantities in the blood vascular system. The right side of the heart and pulmonary artery were distended with bloody froth. The left side of the heart was empty. Air was present in the aorta and its main branches, and beads of air were plainly visible in the coronary arteries, the mesenteric arterioles and such small arteries as were exposed by dissection. The veins everywhere were free from air, except for the portal vein and the great veins near the right side of the heart, which contained large amounts. The left lung was fibrous, contracted and adherent to the wall of the chest throughout, except where there was a small empyema cavity. This cavity communicated with the surface through an old thoracotomy wound. After the left lung was removed, the integrity of its bronchial tree was tested by filling it with water. The water returned immediately by way of the pulmonary vein of the upper lobe. In the left primary bronchus was found a papillary carcinoma nearly obstructing the lumen. On section, the lung proved to be fibrotic throughout and was riddled with saccular bronchiectatic cavities. Dissection failed to show a precise point of communication between the bronchial tree and the pul-

14. Paltauf, quoted from Walcher, K.: *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* 39:314, 1926.

15. Iversen, A.: *Vrtljschr. f. gerichtl. Med.* 22:226, 1862.

16. Lindblom, A.: *Virchows Arch. f. path. Anat.* 252:197, 1924.

17. Neubürger, K.: *Klin. Wchnschr.* 4:113, 1925.

18. Husler, J., and Spatz, H.: *Ztschr. f. Kinderh.* 38:428, 1924.

monary vein, although a clot of fresh blood was found in a bronchiectatic cavity in the upper lobe at a point roughly corresponding to the site of thoracentesis. The right lung was normal, and observations elsewhere were unimportant.

The diagnosis was: carcinoma of the left primary bronchus, bronchiectasis, chronic empyema, bronchovenous fistula and air embolism from the pulmonary vein.

EXPERIMENTAL WORK

Proof by experiment was sought for the theorem suggested by this case: Given a bronchovenous communication, the pressure relationships within the bronchi and veins in a closed chest during life are such as to transfer air from bronchus to vein. Four dogs were used. A bronchovenous fistula was produced within the intact chest in such a manner that communication could be established or abolished at will and the passage of substances through the fistula could be observed.

Dog 1, weighing 10 Kg., was given positive pressure ether anesthesia. The chest was opened through an intercostal incision on the right and the hilum of the lung was exposed. A glass cannula filled with sodium citrate solution was tied into the pulmonary vein of the lower lobe. Another cannula was fixed in the wall of the accompanying bronchus, and the two cannulas were led out of the chest and connected with a short piece of rubber tubing, temporarily clamped off. The lungs were then inflated to exclude pneumothorax and the chest wound closed tightly about the cannulas. The dog was then allowed to recover consciousness fully.

While the animal was walking about, the clamp was suddenly removed from the connecting tube and communication was established between the bronchus and vein. With the next inspiration, the solution in the cannula passed quickly into the vein and was followed by air, as evidenced by the behavior of a little solution that remained in the bend of the tube. The next two or three inspirations each drew more air into the vein, and then the flow was reversed filling the tube with blood. Almost immediately after the first inspiration the dog appeared uncomfortable, and the hind quarters began to drag; paralysis spread and in a few seconds the dog fell to the floor unconscious. There followed focal and general convulsions, labored breathing, extreme rotation of the eyeballs and wide dilatation of the pupils. At about three minutes, muscular relaxation occurred, respirations became feeble and soon ceased. Heart action continued for a minute or so.

Autopsy revealed that the relations within the chest were normal except for the artificial connection between the bronchus and vein. Quantities of air were contained in the vascular system.

DEDUCTIONS

A bronchovenous fistula may be created in man by the passage of an exploring needle into firmly indurated lung tissue. Given such a communication, the relation of bronchial to venous pressures during inspiration is such as to pass air from bronchus to vein and to give rise to fatal air embolism.

DISTRIBUTION OF AIR IN THE CIRCULATION

Gundermann¹⁹ opened the chest of dogs widely with the animals under positive pressure anesthesia and injected air directly into a

19. Gundermann, W.: *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **33**:261, 1921.

pulmonary vein. It appeared to him that the air was distributed by the heart evenly and in proportion to the size among the peripheral arteries, until just before death, when because of a weak heart action the branches of the aorta lying near the heart received a larger share. He observed air bubbles immediately entering the coronary arteries and riding there without a tendency to pass on through the capillaries, and he concluded that air cannot pass any capillary bed. Heller, Mager and von Schrötter,²⁰ on the other hand, observed air bubbles travel through the mesenteric circulation, and Beneke²¹ found air accumulated in large quantities in the right side of the heart, when injection had been made into the peripheral arteries.

That position of the body affects in some degree the distribution of the air in this form of air embolism was suspected by Schlaepfer,²² for he noticed that bubbles could be seen in the retinal vessels of dogs only when the head was held up.

EXPERIMENTAL WORK

The distribution of air received into the pulmonary veins in the vascular tree was studied in dogs under varied circumstances of dosage and body position. The manner of inducing embolism was uniform: With the animals under positive pressure anesthesia, the chest was opened and a glass cannula, filled with sodium citrate solution and temporarily obstructed at the outer end, was fastened in the branch of the pulmonary vein from the lower lobe of the lung and led out of the chest. The chest was closed, residual pneumothorax being avoided. The anesthetic was then discontinued and air was injected through the cannula with a syringe at a uniform rate of 25 cc. per minute. At death, or when the animal was killed, a systematic examination was made of the vascular system.

The experiments may be grouped in accordance with the position of the animal. Representative protocols are as follows:

Group 1: Position Horizontal, Sixty-Seven Dogs.—EXPERIMENT 1.—Dog 21, weighing 16 Kg., was placed on the left side in the horizontal position, and an amount of air equal to 3.9 cc. per kilogram of body weight was injected into the pulmonary vein. Death occurred in nine minutes.

At autopsy, the right side of the heart and adjacent great veins were found moderately distended with air. The pulmonary arteries were filled with air; the left side of the heart and pulmonary veins were free. There were a few air bubbles in the coronary arteries and veins. The aortic arch was partly filled with air, but the descending aorta throughout contained none. The carotid, axillary, internal mammary, intercostal and femoral arteries on the right side

20. Heller, R.; Mager, W., and von Schrötter, H.: *Ztschr. f. klin. Med.* **32**: (suppl.) 113, 1897.

21. Beneke, R.: *Verhandl. d. deutsch. path. Gesellsch.* **16**:263, 1913.

22. Schlaepfer (footnote 6, first reference).

held considerable amounts of air, while the corresponding vessels on the left were relatively free. The mesenteric arteries were beaded with bubbles. Air was found only in the femoral, portal, internal mammary and jugular veins.

In other dogs of this survival time the distribution of air was essentially the same. Those dying more rapidly (in from one to two minutes) showed air still in the left side of the heart and confined largely to the arteries. Little was found in the large veins or right side of the heart. Animals living longer than dog 21 (from twenty to thirty minutes) had little or no air in the right side of the heart and veins and reduced amounts in the peripheral arteries. The coronary arteries were regularly free. A constant and striking observation was unequal distribution, for vessels lying uppermost in the body, here in the right side, were always much more abundantly supplied with air. This evidence of air buoyancy

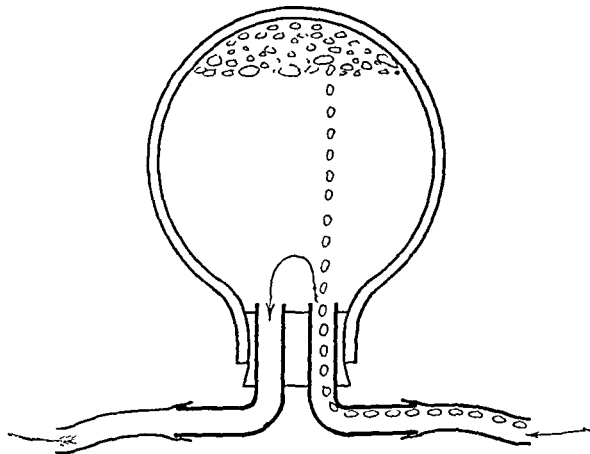


Fig. 1.—Air trap used to study the distribution of air.

was displayed also in the aortic arch. The first portion of the arch lay uppermost and accumulated air from the blood passing through. This air drained off largely into the great vessels of the neck, and the result was to distribute a greater portion of the air to the head, neck and upper extremities than would be indicated from the size of the vessels.

In a few of these dogs, the distribution of air was studied more exactly by interposition of air traps in the blood stream at various points. The air trap (fig. 1) was a small inverted flask with afferent and efferent cannulas. The circulating blood was rendered incoagulable by the intravenous injection of 20 mg. of heparin per kilogram of body weight. The vessel in question was then exposed and divided and the two ends connected with the trap cannulas, the trap being first filled with blood. When adjusted, the trap thus became a part of the vascular system, and by retaining air which passed through the vessel permitted estimation of its appearance time and amount.

EXPERIMENT 2.—Dog 65, weighing 13 Kg., was fitted with traps in both carotid arteries. Three and nine-tenths cubic centimeters of air per kilogram of body weight (50.7 cc.), which is a lethal dose, was injected into the pulmonary vein in the routine manner. Almost instantly after the injection was started air bubbles began to appear in the traps and continued to do so only as long as the injection lasted. The dog recovered; it was killed at one hour.

At autopsy, air was found distributed in the vessels as usual, except that the carotid arteries were free. Twenty-seven cubic centimeters of air was recovered from the traps, i. e., more than half that injected.

EXPERIMENT 3.—Dog 38, weighing 12 Kg., was fitted with traps in both vena cavae, and 3.9 cc. of air per kilogram of body weight (46.8 cc.) was injected into the pulmonary vein. At one minute and twenty seconds, bubbles of air began to appear in the trap of the superior vena cava. No air entered the other trap. Death occurred in ten minutes.

Autopsy showed air to be distributed in the usual manner, except that the right side of the heart and pulmonary arteries were free. Three cubic centimeters of air was present in the trap of the superior vena cava. This amount could obviously not be taken to represent the quantity ordinarily returning to the heart after this dosage of air, since the presence of the traps in the cavae impeded the driving force of the heart to a considerable degree.

Group 2: Position Vertical, Head Down, Sixty-Six Dogs.—Dog 109, weighing 17 Kg., was raised to a vertical position, head down, and 3.9 cc. of air per kilogram of body weight was injected into the pulmonary vein. Death occurred at seventeen minutes.

Autopsy revealed that air filled the coronary arteries and the arteries and veins of the trunk and hind legs. None was found in the vessels of the head, neck and forelegs, nor in the vena cavae, right side of the heart or pulmonary arteries.

In all of these animals, the pattern of distribution was constant. The vessels caudad to the heart alone received air. The coronary arteries contained much more air than with the dog in the horizontal position, and often the blood was entirely replaced by air, giving the vessels the appearance of silver threads. Occasionally, the left ventricle, being inverted, retained a considerable quantity of air indefinitely. No air returned to the right side of the heart.

The observations were corroborated in part by experiments using traps in various vessels.

Group 3: Position Vertical, Head Up, Nineteen Dogs.—Dog 47, weighing 5.5 Kg., was placed in a vertical position, head up, and 3.9 cc. of air per kilogram of body weight was injected into the pulmonary vein. Death occurred in five minutes.

Autopsy revealed that air filled the vessels of the head, neck and forelegs. A small amount was found in the right side of the heart and pulmonary arteries and a few bubbles of air only were contained in the coronary arteries.

In this group of animals again a constant pattern of air distribution was presented, which was complementary in type to that for the group with the head down. Only the vessels taking origin from the aorta cephalad to the heart received air. The coronary arteries were involved to a minimal degree.

DEDUCTIONS

Air that enters the circulation by way of the pulmonary vein follows the course of the blood stream in general but with uneven distribution. Instead of being divided among the vessels in amounts according to their sizes, the air tends to float on the blood and to seek the upper parts of the body. Even where the stream is rapid and violently churned, as in the heart and aorta, air and blood fail to mix thoroughly; the air may remain stationary in a bend of the vessel, or, should gravity so dictate, it may even pass in the direction opposite to that of the blood.

This influence of air buoyancy on the distribution determines distinct differences in various positions of the animal. A typical pattern of embolism with but slight individual variation is found in any given position. Thus, in the dorsal recumbent, horizontal position, air quickly leaves the pulmonary vein and left side of the heart and passes into the aorta. The arch of the aorta is distinctly higher than the descending portion of that vessel and acts as a trap to hold a large part of the air and pass it into the great arch branches. Thus, more than half of the air may go to the head, neck and upper extremities. Distributed in this uneven manner, the air in the form of bubbles is driven to the periphery. The capillaries hinder but do not prevent passage, and after a minute or so air begins to return by the veins of the parts affected to the right side of the heart, whence it is thrown into the lesser circulation. No air succeeds in traversing the pulmonary capillaries but it is held in the pulmonary arterial tree, obstructing the lesser circulation partially and gradually disappearing by excretion into the alveoli and by absorption into the blood and tissues. Air remains longest in the peripheral arteries, sometimes for several hours, for a shorter period in the pulmonary arteries, right side of the heart and great veins, no longer than one-half hour in the coronary arteries and for only a few seconds in the pulmonary veins and left side of the heart. Thus, the period of time that elapses between embolism and death determines largely the position of the air at autopsy.

With the animal in a vertical position, air is distributed only to those parts lying above the level of the heart. Accordingly, when the head is up, the head, neck and forelegs receive the air totally, except for a slight amount in the coronaries; when the head is down, the trunk and hind legs receive the air, and the coronaries are heavily involved.

PHYSIOLOGIC REACTION, TOLERANCE AND CAUSE
OF DEATH

The symptoms in man in air embolism from the pulmonary vein are separable more or less distinctly into two types, neuromuscular and cardiovascular. In a given case, both types may be equally represented, or one may predominate even to the exclusion of the other.

The nervous symptoms are extremely various and occur in different combinations in each instance. The onset may be precipitous with immediate unconsciousness and death, or it may be ushered in more gradually, beginning with dizziness, faintness, local or general paresthesias, aphasia and visual disturbances. More serious symptoms are paraplegia and hemiplegia, blindness, focal and general convulsions, unconsciousness, hyperpnea, Cheyne-Stokes respiration and unequal, dilated and reactionless pupils. Death may occur at any time, and has been known to be delayed as long as six days. When delayed, an unconscious state predominates with periodic convulsions. At any stage, the symptoms may begin gradually to disappear and the patient to recover. Persistent paralyses have occurred.

Cardiovascular symptoms consist in pulse irregularities, asphyxial signs and evidences of gradual or sudden heart failure. Patches of marble-like discoloration are sometimes found on the skin. These symptoms are seen alone when the patient is under general anesthesia and nervous reactions are inhibited, or when the amount of air is overwhelming and nervous effects do not have time to develop. Detailed discussion and illustration of symptoms are given by Schlaepfer.²²

The degree of tolerance in man for air entering the circulation from the pulmonary vein is not known, although it is understood to be much less than that from a peripheral vein. In certain instances, as in the case reported by von Adelung,²³ the amount of gas injected for pneumothorax at the time of air embolism was known, but what part of that actually entered the circulation could not be determined. In animals, Gundermann²⁴ alone has estimated tolerance. Using dogs, he opened the chest with the animals under positive pressure anesthesia and injected air into a pulmonary vein, and found that even 1 cc. slowly introduced was immediately fatal. The unnatural circumstances of the experiments, however, probably rendered the animals abnormally susceptible.

It is generally appreciated that the tolerance of a person for air embolism depends largely on the rate of entrance of air into the circulation.

In air embolism from the peripheral vein the tolerance has been studied experimentally by several investigators. Ilyin²⁴ noted that dogs withstand as much as 2,000 cc. of air injected into the jugular vein at a rate of 30 cc. per minute with 10 mm. of mercury pressure. The dose per kilogram of body weight was not estimated. In twenty-five rabbits, Jehn and Nägeli²⁵ found the maximum tolerance to be 0.89 cc.

23. Von Adelung, E.: A Case of Gas Embolism, *J. A. M. A.* **69**:1522 (Nov. 3) 1917.

24. Ilyin, F.: *J. Akush. i Jhensk. Boliez.* **28**:72, 1913.

25. Jehn, W., and Nägeli, T.: *Ztschr. f. d. ges. exper. Med.* **6**:64, 1918.

per kilogram of body weight; in six cats, 2.5 cc. per kilogram; and of two dogs, one survived 5.3 cc. and one died from 7.7 cc. per kilogram. The rate of the injection was not given. Richter²⁶ stated that in dogs 20 cc. of air produced alarming symptoms and 250 cc. was lethal; in horses, the corresponding amounts were 1,000 and 8,000 cc. No body weights, injection rates or numbers of animals were given. Many other investigators have contributed less accurate data. It is to be concluded that different species present widely different tolerances and among individuals of a single kind there is variation. The values in man are again not known.

The cause of death in air embolism from the pulmonary vein was referred by Gundermann¹⁹ to heart failure, after observing in his dogs immediate myocardial incapacity following the entrance of air into the coronary arteries. He pointed out that heart action ceased too soon to allow involvement of the brain to play a part. Beneke,²⁷ at autopsy in man, found much air in the right side of the heart and pulmonary arteries and suggested that death was due to obstruction of the lesser circulation, as in air embolism arising from a peripheral vein. The fallacy of this assumption was indicated by Gundermann in the fact that an amount of air which is lethal when entering the pulmonary vein is readily tolerated when injected into a peripheral vein. The majority of authors agree with Brauer²⁸ and his school in ascribing death to brain embolism, since nervous symptoms frequently predominate and at death respirations usually cease long before heart action. Wever²⁹ injected air into the carotid artery of dogs and monkeys and produced a symptom complex similar to that of man. The brains of Wever's animals were examined by Spielmeyer.³⁰ Those that survived more than fifteen hours presented focal ischemic necrosis distributed irregularly, chiefly in the cerebral cortex, and characterized by degenerative alterations in the ganglion cells and glial proliferation. The degree was in proportion to the amount of air and to the period of time between embolism and death. The same changes were found in cases in man. Gold³¹ described the brain of a person who died six days after cerebral air embolism, and in addition to the alterations mentioned, indicated edema of the whole brain and petechial hemorrhages in the medulla oblongata and pons.

26. Richter, quoted from Hutter, K.: *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* 40:131, 1927.

27. Beneke, R.: *Beitr. z. Klin. d. Tuberk.* 9:343, 1908.

28. Brauer (footnote 2, second reference).

29. Wever (footnote 6, second reference).

30. Spielmeyer, W.: *Verhandl. d. Kong. f. inn. Med.* 30:359, 1913.

31. Gold, E.: *Arb. a. d. neurol. Inst. a. d. Wien. Univ.*, 1924, vol. 26.

CLINICAL CASES

Case 1, already described, illustrates the purely cardiovascular type of symptomatology, and case 2, to be described, the neuromuscular type.

EXPERIMENTAL WORK

Physiologic Reaction.—The reaction of the dog to air injected into the pulmonary vein was studied under varied experimental circumstances. The doses, determined according to the body weight, ranged from amounts easily borne to those immediately fatal. Three positions were employed, as in the preceding experiments. The method was the same in all instances:

A cannula was placed in a pulmonary vein. The femoral artery was cannulated and connected with a mercury manometer. With the

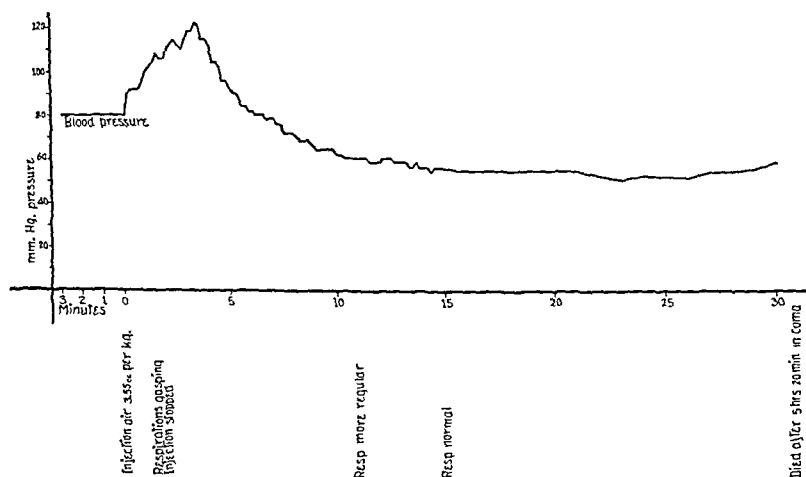


FIG. 2 (dog 20).—Injection of air into the pulmonary vein, with the dog in the horizontal position. Moderately severe reaction.

animal under ether anesthesia, respiration and blood pressure were observed, and when they had been constant for three minutes, the ether mask was removed and the dose of air injected into the cannula of the vein at a rate of 25 cc. per minute. The reaction was noted in detail.

Typical protocols are as follows:

Group *a*: Position Horizontal, Sixty Dogs: EXPERIMENT 1.—Dog 20, weighing 16 Kg., received 3.55 cc. of air per kilogram of body weight and displayed a moderately severe reaction (fig. 2).

At one minute thirty seconds, respiration became gasping and irregular; at eleven minutes, more regular, and at fifteen minutes, normal.

At two minutes, the injection of air was complete.

At three minutes twenty seconds, the blood pressure, which had begun to rise with the beginning of the injection of air, reached a maximum of 40 mm. of

mercury above normal. It then fell gradually to a minimum of 30 mm. of mercury below normal at twenty-three minutes. It was commencing to rise when the readings were stopped.

The pulse was regular and strong throughout.

Unconsciousness continued, although no more anesthesia was administered. After one hour twitching contractions of the legs and walking movements began. The muscles were spastic and at times the decerebrate posture of Sherrington was assumed. The dog moaned and howled now and then, although obviously unconscious. No cardiorespiratory irregularities were noted. After four hours, consciousness returned sufficiently to permit vague recognition of surroundings and unsteady walking, but this was temporary and death occurred in deep unconsciousness at five hours twenty minutes.

EXPERIMENT 2.—Dog 28, weighing 22 Kg., received 3.9 cc. of air per kilogram of body weight and presented a severe reaction (fig. 3).

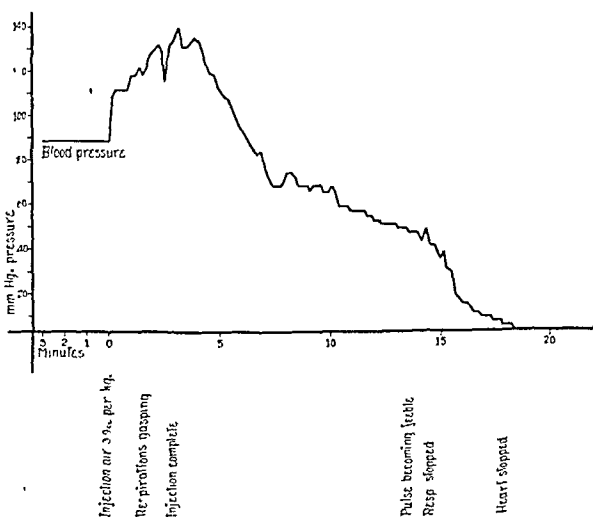


FIG. 3 (dog 28).—Injection of air into the pulmonary vein, with the dog in the horizontal position. Severe reaction.

At two minutes, respirations were gasping. There were periods without breathing. At fifteen minutes, breathing ceased.

At three minutes twenty seconds, the injection of air was complete.

At three minutes ten seconds, the blood pressure, which began to rise with the injection of air, reached a peak of 52 mm. of mercury above normal, and then fell jerkily to 0 at eighteen minutes twenty seconds.

The pulse remained regular and full until the fourteenth minute, when it became increasingly feeble; it ceased at eighteen minutes twenty seconds.

Others of these dogs, receiving smaller doses, showed reactions during the first half hour similar to those of dog 28, but less severe and usually followed by recovery. There was always a period of unconsciousness beyond that to be expected from the anesthetic.

Group *b*: Position Vertical, Head Down, Thirty-Two Dogs: EXPERIMENT 1.—Dog 70, weighing 23.6 Kg., received 1.22 cc. of air per kilogram of body weight and presented a moderately severe reaction (fig. 4).

Respirations were affected at no time.

At one minute, the injection of air was complete.

At ten seconds, the blood pressure rose 20 mm. of mercury, dropped almost immediately and remained about 10 mm. of mercury below normal.

At fourteen minutes, the pulse, thus far regular and strong, suddenly began to skip beats, often two or three together, and blood pressure took wide drops. This irregularity continued twenty minutes and suddenly stopped. The pulse continued normal.

At five minutes, consciousness began to return and ether had to be readministered. At thirty minutes, ether was discontinued and the apparatus disconnected. The dog began to awaken as ordinarily from anesthesia and showed no effects of embolism.

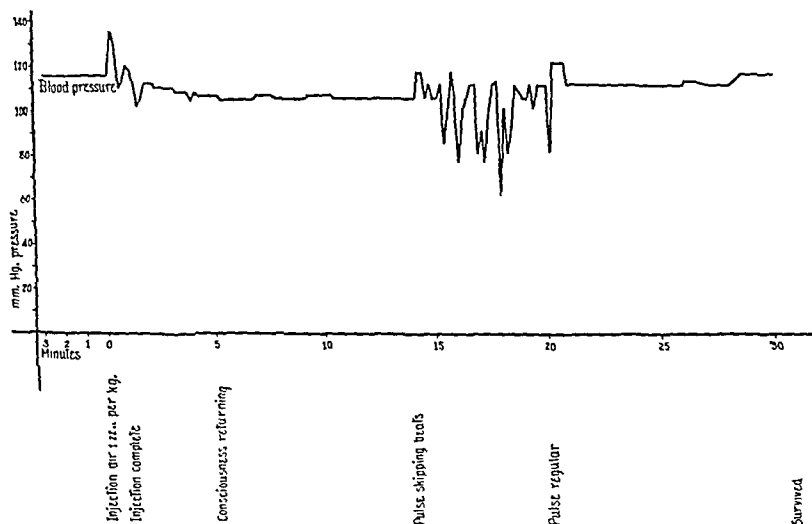


FIG. 4 (dog 70).—Injection of air into the pulmonary vein, with the dog in the head-down position. Moderately severe reaction.

EXPERIMENT 2.—Dog 66, weighing 18.1 Kg., received 1.22 cc. of air per kilogram of body weight and had a severe reaction (fig. 5).

Respirations were normal until the fourteenth minute, when they abruptly failed and represented the last sign of life.

At one minute, the injection of air was complete.

At twenty seconds, the blood pressure was 20 mm. of mercury above normal. It dropped slightly and then rose to a level of from 10 to 15 mm. of mercury above normal. At thirteen minutes, the heart action, which had till then been strong and full, suddenly failed and the blood pressure dropped precipitously to 0 at fourteen minutes.

Dogs in this position showed only cardiovascular symptoms. Heart block was frequent and characteristic and was the cause of death, rather than the gradual myocardial failure seen in the horizontal position.

With large doses, sudden, total block occurred very early; with smaller amounts, total block appeared as abruptly but after from ten to twenty minutes of fairly normal course immediately preceded or not by a few dropped pulse beats, or a period of dropped beats (partial block) came and went without warning, followed by recovery. No heart block was initiated after thirty minutes. In none of the animals were there signs of involvement of the central nervous system. There was no interference with consciousness.

Group *c*: Position Vertical, Head Up, Eighteen Dogs: Dog 48, weighing 9.1 Kg., received 3.9 cc. of air per kilogram of body weight and presented a severe reaction (fig. 6).

At thirty seconds, the respirations were shallow and gasping; they ceased at one minute.

At one minute ten seconds, the injection of air was complete.

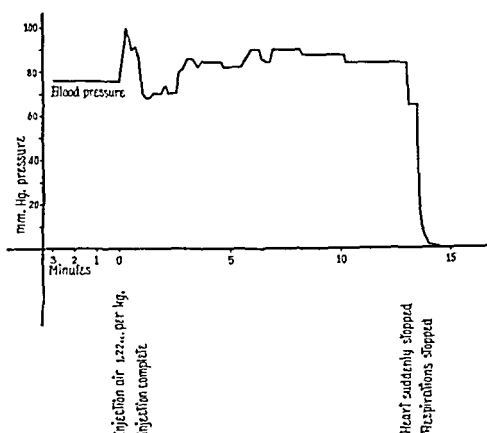


FIG. 5 (dog 66).—Injection of air into the pulmonary vein, with the dog in the head-down position. Severe reaction.

At twenty seconds, the blood pressure had risen to 38 mm. of mercury; it dropped immediately to 0 at four minutes.

At two minutes, the pulse became weak, and the heart action ceased at four minutes as the last sign of life.

Other dogs that received smaller doses exhibited less severe reactions, but none recovered. The respirations were almost instantly affected and permanent cerebral injury with unconsciousness occurred with the smallest doses. The heart showed no disturbance until some time after respirations ceased.

Group *d*: Investigation of Blood Pressure Reaction, Ten Dogs: The cause of the initial elevation in blood pressure that appears characteristically in air embolism from the pulmonary vein was investigated. Possible causes for this are direct cardiac effects, action on the central nervous system and action directly on the blood vessels. The last

appeared the most likely, for air accumulates in the peripheral arterioles and capillaries and probably increases resistance to blood flow. The first two possibilities were eliminated by experiment, as follows:

With the animals under ether anesthesia, a cannula was inserted in an intercostal artery, pointing toward the aorta. With the dog horizontal, air was injected through the cannula and intercostal vessel into the descending aorta at a rate of 25 cc. per minute. Various doses of air were employed.

Dog 40, weighing 22.4 Kg., received 3.9 cc. of air per kilogram of body weight (fig. 7).

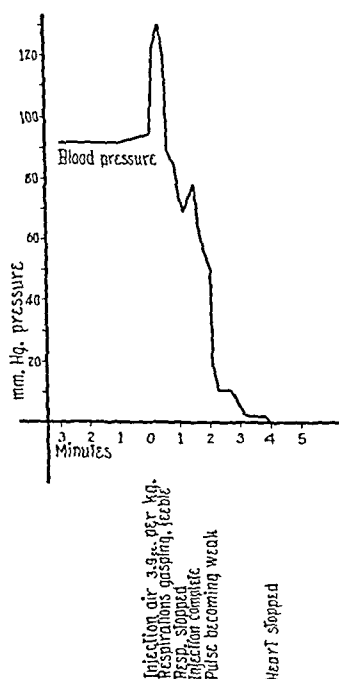


FIG. 6 (dog 48).—Injection of air into the pulmonary vein, with the dog in the head-up position. Severe reaction.

The respirations and pulse were affected at no time.

The blood pressure commenced to rise immediately after the injection was started and reached 40 mm. of mercury above normal at thirty seconds. This elevation was maintained for five minutes, when the pressure returned to normal. At three minutes thirty seconds, the injection of air was complete.

Autopsy showed no air to have entered the coronary arteries or vessels of the head, neck and forelegs.

Tolerance.—The tolerances for air injected into the circulation at various points were compared:

With the animals under ether anesthesia, the pulmonary vein was cannulated in twenty-one dogs, the jugular vein in twenty-six dogs and

the seventh intercostal artery (descending aorta) in ten. Into each dog was injected an amount of air determined according to the body weight and varied from dog to dog, with the purpose of finding the maximum tolerance dose. The rate of injection was 25 cc. per minute. After four hours the outcome was noted, whether by death or by recovery.

The results are charted in figure 8. Here each of three columns represents the greatest amount of air per kilogram of body weight withstood in one of the forms of air embolism. The figures inserted in each column specify the numbers of dogs used, and the positions of the figures indicate the doses and the fates of the dogs. Thus, the maximum tolerance dose for the pulmonary vein is 1.5 cc. per kilogram, while those for the jugular vein and descending aorta are .76 and .70

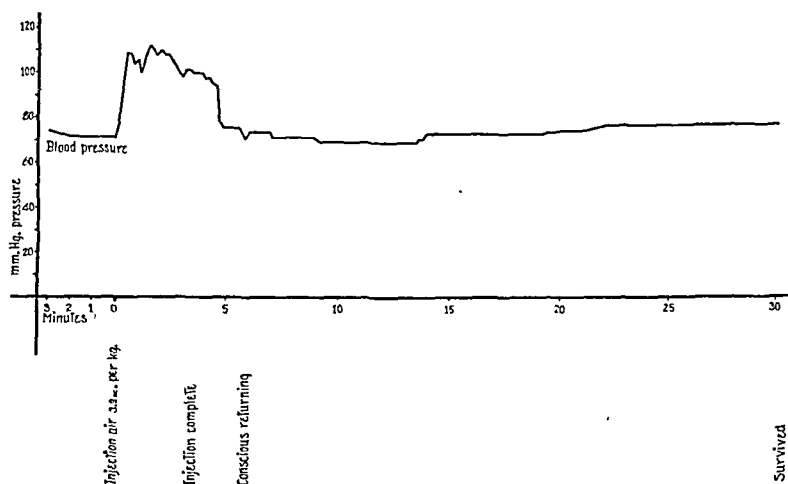


FIG. 7 (dog 40).—Injection of air into the intercostal artery (aorta), with the dog in the horizontal position.

cc., or at least fifty times as great. Considerable individual variation is evident.

The tolerance for air injected into the pulmonary vein was determined for various positions of the body, with twenty-one dogs in the horizontal position, seventeen with the head up and thirty-two with the head down.

The results are charted in figure 9, the same method being employed as for the preceding chart. The maximum tolerance dose is 0.5 cc. per kilogram of body weight with the head up, 1.5 cc. or three times as great in the horizontal position, and 3.3 cc. or six and one half times as great with the head down. Individual variation presents itself.

Cause of Death.—The observations recorded concerning the symptomatology and distribution of the air suggest that the cause of death differed in certain body positions. With the head up, the air ascended

and involved the brain massively. Death resulted either early from respiratory failure (embolism of the medulla oblongata) or, later from decerebration.

In the head-down posture, the air ascended caudally. The coronary arteries were affected most seriously. The heart instantly ceased to beat or, with smaller doses, it continued for a few minutes and then underwent heart block. The brain was protected from embolism and played no part in the cause of death.

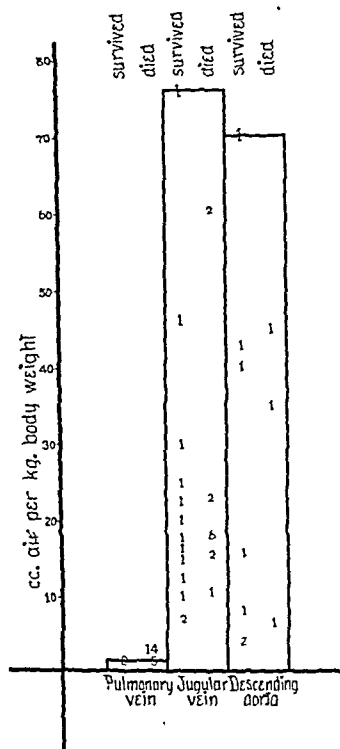


FIG 8.—Tolerance for air injected into the circulation at various points.

In the horizontal position, the air passed to both brain and coronary vessels. In certain instances, the symptoms preceding death suggested involvement of the brain as the lethal factor; in others, coronary involvement. To test the relative importance of these two factors in this position, experiments were devised wherein the brain was protected from air embolism:

With the animals under ether anesthesia, air traps were placed in both carotid arteries. Both vertebral arteries were ligated. A strand of wire was twisted tightly about the neck, including all structures except the carotid arteries, jugular veins, vagus nerves and trachea. Thus, the only blood supply remaining to the brain was through the

trapped carotid vessels. Three and nine-tenths cubic centimeters of air per kilogram of body weight, which is a lethal dose, was then injected into a pulmonary vein. Seven dogs were used.

Dog 32, weighing 11.5 Kg., did not present symptoms referable to embolism. The animal recovered. At one hour, the dog was killed.

Autopsy revealed that the distribution of air was typical of that of pulmonary vein air embolism in this position, except that the head and neck were free. The traps contained 32 cc. of air.

In one other dog, the result was the same. In five dogs, death occurred within a few minutes after embolism.

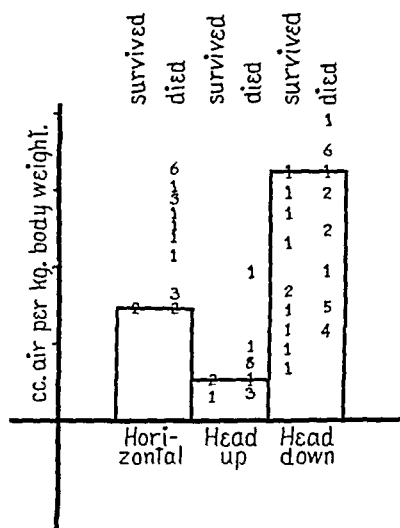


FIG. 9.—Tolerance for air injected into the pulmonary vein in various positions.

DEDUCTIONS

These animals were under general anesthesia at the time of the injection of air, and during the first ten to twenty minutes the symptomatic effects of embolism of the higher brain centers were necessarily eliminated. This part of the picture is supplied, however, in the experiments in the section on etiology.

The symptomatology was found to be similar in all details to that in man, and to be separable into two types, i.e., neuromuscular and cardiovascular. Extreme variation in appearance and degree also occurred, even with the same amounts of embolus.

There were two well defined periods in the reaction, acute and chronic. The acute period lasted up to one-half hour and was characterized by disorders of respiration, heart function and blood pressure, together with irritative and paralytic effects in the higher brain centers.

The chronic period presented states of semidecerebration or total decerebration, delirium, semilucid periods and convulsive seizures. Improvement leading to recovery was seen at any stage but was rare after three hours. The severity of symptoms was in proportion roughly to the amount of embolus; death occurred in either period.

The type of symptoms was determined largely by the position of the animal. In the vertical position, head up, the neuromuscular type was dominant, and the only cardiovascular effect detectable was the elevation of the initial blood pressure. In the vertical position, head down, cardiovascular responses alone appeared. With the dog horizontal, both types occurred and in varying proportions but the neuromuscular usually predominated.

A constant symptom was the elevation of the initial blood pressure. Evidence was obtained that this resulted from the accumulation of air bubbles in the peripheral arterioles and capillaries with increased resistance to arterial blood flow.

The tolerance of the dog for air injected into the circulation depends largely on the portal of entry. In the jugular vein or descending aorta more than fifty times as much may be withstood as in the pulmonary vein. In the pulmonary vein tolerance depends on body position, and is least in the head-up position, three times as great in the horizontal and six and one-half times as great in the head-down position.

The fatal effects of air embolism from the pulmonary vein are due to impairment of three vital functions; i. e., cardiac activity by the obstruction of the coronary arteries, cerebral and medullary function by blockage of the arteries of the brain and blood circulation by blockage of the pulmonary arteries. Either the first or the second may be the primary cause of death; the third is never more than contributory. The first is the sole cause of death when the animal is in the head-down posture and the mechanism is by heart block; the second alone causes death when the animal is situated head up, with respiratory paralysis in the early stage or decerebration later; in the horizontal position all three contribute and the first or the second may be primary, depending on the chance distribution of the air embolus.

DIAGNOSIS AND PROGNOSIS

The diagnosis of air embolism from the pulmonary vein has been made without difficulty when sucking was heard at an open vessel or when gas was injected into the chest immediately before the symptoms. Becker,³² Stargardt,³³ Perthes³⁴ and others have been led by the visual

32. Becker, E., quoted from Brauer, L.; Schröder, G., and Blumenfeld, F.: *Handbuch der Tuberkulose*, ed. 3, Leipzig, J. A. Barth, 1923, vol. 2, p. 461.

33. Stargardt, quoted from Gundermann, W.: *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* 33:261, 1921.

34. Perthes, quoted from Gundermann, W.: *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* 33:261, 1921.

disturbances in some of these cases to examine the eyegrounds and were able to establish a diagnosis by seeing bubbles in the retinal vessels. A large proportion of the cases, however, have probably remained obscure from lack of direct evidence. Often the portal of entry of air or gas into the circulation was not apparent, nor was there a sucking sound; no heart murmur occurred to point to the diagnosis, as in air embolism from a peripheral vein; an ophthalmoscope has rarely been at hand.

The symptomatology has not assisted greatly in diagnosis, due to confusion with that of other forms of sudden collapse, i.e., internal hemorrhage, surgical shock, heart failure, the syncope that ensues with the rapid removal of much fluid from the pleural cavity and pleural reflex. The last of these, otherwise known as pleural eclampsia or pleural shock, has contributed chiefly to the confusion, for it is believed by many that nerve impulses elicited from the pleura and lung by trauma from an instrument are capable of producing all symptoms seen in air embolism. The nature of such nerve reflexes has been studied. Brodie and Russell³⁵ demonstrated strong vagal responses in animals obtained by stimulation of vagal fibers at the hilum, bronchi and alveoli of the lung. Sauerbruch³⁶ saw sudden heart failure in man immediately following mass ligation at the hilum of the lung or probing within a bronchial fistula. Johnson and Luckhardt³⁷ found that sudden, forceful inflation of the lungs in man and animals results in vagus reflex that profoundly slows the heart and depresses the blood pressure, often fatally, and Johnson and Van Allen³⁸ proved that this reflex originates from the vagus fibers in the lung. Moreover, the experimental work of Capps and Lewis³⁹ indicated the presence of two powerful reflexes, one vagal and resulting in cardiac inhibition and the other vasomotor with dilator influence on the peripheral vessels. These could be obtained separately or at once by irritation of the inflamed but not of the normal pleura. The cardio-inhibitory reflex was in itself insufficient to cause death but the vasomotor effects were frequently not recovered from; both served to lower the blood pressure profoundly. Thus, it is proved that what may be termed pleural reflex exists in both man and animals and that inhibition of the heart rate, peripheral vasodilatation and fall in the blood pressure occur and may result in death. On the other

35. Brodie, T., and Russell, A.: *J. Physiol.* **26**:92, 1900.

36. Sauerbruch, F.: *Chirurgie der Brustorgane*, Berlin, Julius Springer, 1925, vol. 2, p. 160.

37. Johnson, C. A., and Luckhardt, A. B.: *Am. J. Physiol.* **83**:642, 1928; *ibid.* **84**:453, 1928.

38. Johnson, C. A., and Van Allen, C. M.: Unpublished work.

39. Capps, J. A., and Lewis, D. D.: *Am. J. M. Sc.* **134**:868, 1907; *Blood-Pressure-Lowering Reflexes from Irrigation of the Chest in Empyema*, *Arch. Int. Med.* **2**:166 (Sept.) 1908.

hand, no matter how profound these effects have been, no one has obtained focal irritative and paralytic phenomena of the brain such as occur commonly in cerebral air embolism. In this connection it is to be emphasized that in the lung inflation phenomenon of Johnson and Luckhardt the cerebral symptoms were shown to be the result of ischemia of the brain and without relation to the vagal reflex.³⁸ Disregarding these facts, two extreme and opposite views are held as to the cause of these obscure cases of sudden collapse following instrumentation of the lung. The majority of authors, as Forlanini,⁴ Saugmann⁴⁰ and Stivelman,³ diagnose pleural reflex and pay little or no attention to the possibility of air embolism, while others, notably Brauer,²⁸ Wever²⁹ and Schlaepfer,²² as consistently ascribe the condition to air embolism.

All characteristic symptoms that have been noted in this form of air embolism failed when the subject was under general anesthesia or when the air entered rapidly and in large amounts, since no opportunity was given for evidence of involvement of the brain. The picture was simply that of sudden heart and respiratory failure.

The diagnosis made at autopsy of air embolism from the pulmonary vein has depended on the demonstration of air in the blood stream or of typical cerebral lesions. Both of these could not appear in the same body, since air remains in the vessels during life a few minutes or hours only and the degenerative changes in the brain from embolism develop only after fifteen hours.³⁰ Thus, patients in whom death occurs between two and fifteen hours after the onset of symptoms are expected not to exhibit at autopsy evidence of air embolism, either in the form of intravascular air or that of secondary changes in the brain. Moreover, very small amounts of air may be lethal in embolism from the pulmonary vein, and even though death occurs at once its demonstration in the peripheral vessels is difficult. Use of the roentgen rays has been proposed for diagnosis.⁴¹

Richter⁴² described a technic for the demonstration of air or gas in the vessels at death which has become standard. Each organ is isolated *in situ* by ligation of the vessel supply, then removed and incised under water. Air escaping from the tissues bubbles up plainly. The heart is managed somewhat more simply, for ligation and removal is dispensed with. The pericardium is opened and held suspended to serve as the dish for water submersion. Objection has been raised to this method as laborious and misleading, for the air may be withheld in the vessels by clots and fail to bubble forth, and the water quickly

40. Saugmann, C.: *Beitr. z. Klin. d. Tuberk.* **31**:571, 1914.

41. Baum, F.: *Am. Med.* **33**:271, 1927.

42. Richter, M.: *Gerichtsärztliche Diagnostik und Technik*, Leipzig, S. Hirzel, 1905.

becomes bloody and obscures the tissues. Moreover, direct observation of the vessels serves to detect even very small amounts of air, since the smaller arterioles are translucent enough to show air bubbles distinctly and the air in larger vessels, heart, cavae and aorta, is present in the form of froth and escapes as such plainly when the lumen is opened.

It is well known that little significance can be placed on finding air bubbles in the cerebral vessels at autopsy, unless great care has been taken in exposing the brain. In lifting off the skull cap, as it is routinely carried out, cortical vessels are stretched and ruptured and air is sucked from the atmosphere into their lumina.

Differentiation at autopsy of the type of air embolism has depended on three things. 1. The vessel that served as portal of entry is sought. 2. The distribution of the air is determined, the fact being borne in mind that the lesser circulation acts as an effectual barrier to air bubbles. Thus, if air was found in the left side of the heart or the peripheral arteries, the case was one of embolism from the pulmonary vein; if only in the large veins, right side of the heart and pulmonary arteries, it was embolism from a peripheral vein. One exception has pertained to this; a patent foramen ovale may allow air to pass from the right to the left side of the heart and differentiation is prevented. 3. The typical cerebral degenerative lesions are sought for and indicate the pulmonary vein type of embolism, unless there is a patent foramen ovale.

It has been emphasized that fallacious conclusions may result from the presence of putrefactive gases in the blood at autopsy. Dyrenfurth⁴³ found by actual measurement that within twenty-four hours amounts of gas up to 0.25 cc. may be present in the heart cavity, and that this may increase during the next few days to 4 cc. In air embolism from a peripheral vein there was regularly as much as 7 cc., but this is probably too high for embolism from the pulmonary vein, where smaller amounts are lethal. Dyrenfurth⁴⁴ devised a method for the qualitative test of these gases, to rule out the putrefactive. Simmonds⁴⁵ recommended culture of the heart blood for the presence of gas-forming organisms, for the same purpose.

Prognosis has been uncertain. Usually, the return of consciousness has indicated improvement leading to recovery, but in some cases consciousness has been recovered only for relapse to occur. In recovery after pronounced symptoms, focal paralyses lasting as long as six months have been seen.⁴⁶

43. Dyrenfurth, F.: *Med. Klin.* **22**:807, 1926.

44. Dyrenfurth, F.: *Deutsche Ztschr. f. d. ges. gerichtl. Med.* **8**:727, 1926.

45. Simmonds, M.: *München. med. Wchnschr.* **62**:662, 1915.

46. Head, J.: Personal communication to the authors.

EXPERIMENTAL WORK

Diagnosis.—A characteristic sign of air embolism from the pulmonary vein, noted practically always in these experiments, was immediate elevation of the arterial blood pressure. The most frequent degree of rise was from 30 to 40 mm. of mercury, but often the initial pressure was more than doubled. The elevation was maintained as long as air continued to be injected and usually also for a minute or two afterward. Even exceedingly small amounts of air produced detectable hypertension. In air embolism from the peripheral vein, on the other hand, initial depression of the blood pressure is the rule. These opposite effects are illustrated in the following experiment.

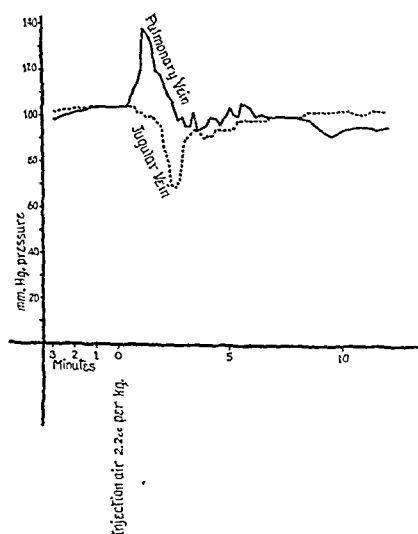


FIG. 10 (dog 6).—Injection of air into the pulmonary vein, followed in thirty minutes by the injection of air into the jugular vein (graphs superimposed).

Dog 6, weighing 8.4 Kg., was fitted with cannulas in both pulmonary and jugular veins. The femoral artery was connected to a mercury manometer and the normal blood pressure level was recorded. Then a small amount of air (2.2 cc. per kilogram) was injected into the pulmonary vein and the blood pressure reaction noted. Forty-five minutes later, when the pressure was again at a normal level, the same amount was injected into the jugular vein, and the reaction again noted.

The two blood pressure curves thus obtained are compared in figure 10 by superimposition. One is seen to be the reverse of the other.

A second characteristic sign of air embolism from the pulmonary vein is elicited as follows: A stab cut is made through the skin of a part of the body that is uppermost and bleeding is produced. Bubbles of air will stream out distinctly with the blood. The test should be made within fifteen minutes after embolism.

Prognosis.—Prognosis in air embolism from the pulmonary vein in the dog was possible within certain limits: 1. The severity of the symptoms depended in general on the amount of air entering the circulation. 2. Primary respiratory failure was looked for only within the first ten to fifteen minutes; primary heart failure, within half an hour. 3. Unconsciousness, when continued longer than half an hour, indicated serious cerebral involvement.

CLINICAL CASES

Case 2 illustrates the use of the blood pressure reaction in the diagnosis of air embolism in man.

CASE 2.—A white woman, aged 51, presented an illness of seven months' duration. The onset was sudden, with chills, fever and pain in the left side of the chest. Cough developed and fever continued for three weeks. There had been continuous cough and intermittent periods of fever since then. There was 250 cc. of foul sputum daily, which was negative for tubercle bacillus. A moderate loss of weight and strength occurred. The diagnosis was chronic abscess of the left lung.

The patient was admitted to University of Iowa Hospital, surgical service. Iodization of the bronchial tree showed a large filling in the center of the left lung, extending laterally to within 2 cm. of the pleura. This was interpreted as an abscess cavity.

On two occasions attempts were made to reach the abscess with an exploratory needle, without success. The third attempt was as follows: With the patient under local anesthesia, the third rib was resected in the anterior axillary line, which was a point shown by fluoroscopy to overly the abscess closely. The pleura was found free, and the wound was packed with gauze to produce adhesions. Four days later, the pack was removed and exploration was performed without anesthesia, the patient sitting semi-erect. A large hypodermic needle, attached to a syringe, was passed perpendicularly through the rib bed into the lung. The parenchyma was found to be tough. Nothing could be aspirated, except that at one point blood was freely drawn and at another air. The puncture was repeated, and at a depth of 5 cm. the patient started to cough. The needle was withdrawn. She raised a little bright frothy blood and continued to cough urgently. She experienced a prickling sensation over the body surface and became unable to speak. Dyspnea developed and, at about one minute, unconsciousness. The pulse rate was 66, and was slightly irregular. The color was somewhat cyanotic. At about ten minutes (accurate time is not kept at such emergencies) the blood pressure was taken and found to be 180 systolic and 80 diastolic; at twenty minutes, 162 systolic and 76 diastolic; at thirty minutes, 152 systolic and 70 diastolic; at forty minutes, 140 systolic and 68 diastolic; at fifty minutes, 130 systolic and 65 diastolic, and seventy-five minutes, 125 systolic and 65 diastolic. Consciousness returned at thirty minutes and with it speech; at this time it was noted that the entire left side of the body was paralyzed and with hyperactive tendon reflexes. There was no anesthesia. The eyegrounds were normal. At forty-five minutes, the paralysis began to disappear and cleared at one hour. A sensation of heaviness persisted in that side of the body. Dyspnea gradually disappeared. After one and one-half hours the condition was normal, except for the pulse rate, which was 120.

It was thought that air embolism from the pulmonary vein was the cause of the condition, since: 1. Needle puncture in a sclerotic lung is known (case 1) to be capable of producing a bronchovenous fistula, and such a communication permits air to be inspired into the circulation. Here a bronchus and blood vessel are known to have been pierced in a sclerotic lung. 2. During the height of the reaction the blood pressure was found markedly elevated, and in no other form of sudden collapse, save cerebral hemorrhage, is this seen. 3. The symptoms were chiefly those of transient cerebral dysfunction characteristic of air embolism of the brain.

DEDUCTIONS

The diagnosis of air embolism from the pulmonary vein is assisted by two phenomena, readily elicited:

1. Initial elevation of the blood pressure: In the dog, this lasts as long as air continues to enter the circulation and heart action is maintained. Even very small amounts of air produce noticeable elevation. In man, the reaction is described, and here the elevation was maintained about one hour. The presence of this phenomenon in cases of sudden collapse with instrumentation of the lung rules out air embolism from a peripheral vein, pleural and vagal reflex, hemorrhage and traumatic shock. Its transiency rules out cerebral hemorrhage.

2. "Air bleeding": In air embolism from the pulmonary vein, the peripheral capillaries in the upper parts of the body contain bubbles of air, and these flow plainly out with the blood from a wound. A small stab incision serves to demonstrate this. The phenomenon is pathognomonic.

Prognosis is difficult; it depends on appreciation of the amount of air embolus, severity of symptoms and the time interval.

PREVENTION

Measures to insure against air or gas embolism during the administration of artificial pneumothora, particularly at the initial filling, have eliminated much of the danger. Thus, there is the incision method of Brauer,⁴⁷ employment of a blunt needle, manometer control, etc. The accident occasionally takes place, however, even in the best hands.

During the irrigation and probing of pleural fistulas, it has been advocated⁴⁸ that no injury, either by direct trauma or by stretching, be inflicted on the pleural surface or pleural adhesions. Instances of shock following such procedures have been accompanied by bleeding as evidence of damage to vessels within the sinus.

47. Brauer, L., and Spengler, L.: *Beitr. z. Klin. d. Tuberk.* **14**:419, 1909.

48. Schlaepfer, K.: *Surg. Gynec. Obst.* **37**:510, 1923.

Spontaneous suction by a pulmonary (or other) vein of air from the outer atmosphere is prevented with certainty by causing the patient to breathe under positive pressure at the time, as demonstrated by Tiegel in 1907.⁴⁹ The principle of the apparatus necessary for this purpose is illustrated in figure 11.

EXPERIMENTAL WORK

Various measures that might be expected to prevent spontaneous air embolism from the pulmonary vein were tested in the dog, (1) under the conditions of external venous fistula and (2) under conditions of bronchovenous fistula.

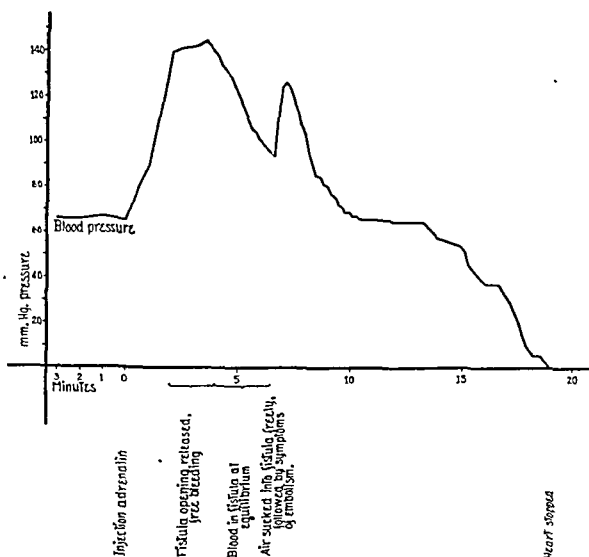


FIG. 11 (dog 50).—Pulmonary vein fistula; temporary protection against air suction by the injection of epinephrine.

External Fistula.—(a) Positive Pressure Breathing, Two Dogs: Dog 49, weighing 8.5 Kg., was anesthetized and fitted with a pulmonary vein cannula. Placed in the horizontal position, positive pressure breathing was applied.

At 20 cm. of water pressure, the cannula was opened. The blood from the vein flowed freely out, both in inspiration and in expiration.

At 17 cm. of water pressure, the bleeding was less free.

At 14 cm. of water pressure, bleeding occurred during expiration, and the column of fluid in the cannula remained stationary in inspiration. At 11 cm., the column of fluid was stationary in expiration and dropped toward the vein slightly in inspiration.

At 8 cm., the fluid meniscus appeared above the surface of the chest in expiration and dropped below in inspiration.

At 5 cm., the fluid remained always below the surface of the chest but embolism did not occur.

49. Tiegel, M.: Mitt. a. d. Grenzgeb. d. Med. u. Chir. 3:789, 1907.

At 3 cm., air was drawn freely through the cannula, and the animal died of air embolism.

(b) Intravenous Injection of Epinephrine, Four Dogs: Dog 50, weighing 5.8 Kg., was placed under general anesthesia, in the horizontal position, and was fitted with a pulmonary vein cannula and a femoral blood pressure recording apparatus. The normal pressure was recorded, and then 0.5 cc. of epinephrine hydrochloride was injected intravenously (fig. 11).

At injection, the blood pressure started to rise.

At two minutes, when the pressure was 74 mm. of mercury above normal, the cannula was opened and found to bleed freely.

The pressure continued to rise and then fell gradually with constant tendency to bleed from the cannula.

At four minutes ten seconds, when the pressure was 72 mm. of mercury above normal, equilibrium was reached. As the pressure fell further the meniscus in

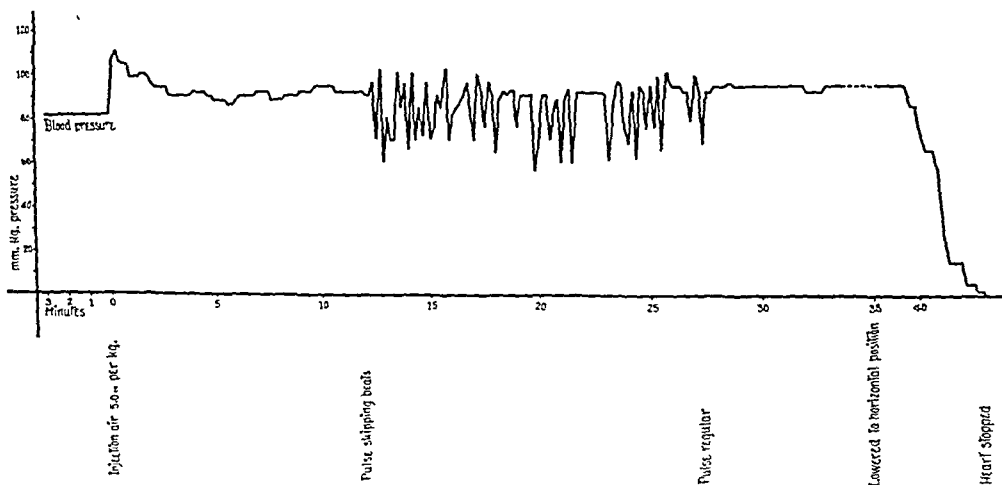


FIG. 12 (dog 111).—Injection of air into the pulmonary vein, with the dog in the head-down position. Illustrating the fatal effect of resuming the horizontal position too soon.

the cannula dropped, and at six minutes thirty seconds, at 28 mm. of mercury elevation, there was sucking of air into the vein, and the dog died from embolism.

In other dogs, the effect was similar, although the blood pressure values were different in each case. Ephedrine was found to act in the same manner.

Bronchovenous Fistula.—(a) Positive Pressure Breathing, One Dog: In dog 51, weighing 6.9 Kg., while under general anesthesia, a bronchovenous fistula was created as in dog 1 (section on etiology) and the communication was kept blocked at first by clamping the U-tube. Positive pressure breathing was applied. At 10 cm. of water pressure, the clamp was removed and patency of the fistula was established. Air passed immediately from bronchus to vein, and the dog died.

(b) Negative Pressure Breathing, One Dog: Dog 52, weighing 7.5 Kg., was treated in a similar manner to dog 51, except that negative pressure breathing

was administered. At 24 cm. of water pressure, the clamp was removed from the U-tube. Air passed rapidly from the bronchus to the vein. The dog died.

(c) Intravenous Injection of Epinephrine, Three Dogs: Dog 53, weighing 9.2 Kg., was fitted with a bronchovenous cannula and a femoral blood pressure recording apparatus. The normal pressure was determined and then 0.5 cc. of epinephrine hydrochloride was injected intravenously.

At injection, the blood pressure began to rise.

After one minute and fifty seconds, with the pressure 56 mm. of mercury above normal, the U-tube was released. The venous blood flowed quickly toward the bronchus.

The pressure continued to rise and then fell gradually, with a constant tendency to bleed from the vein.

After four minutes, the pressure reached 14 mm. of mercury above normal and air was drawn with each inspiration from bronchus to vein, with death.

A similar, transient protection against embolism was seen in the other dogs.

Bronchus Block, Three Dogs: Dog 54, weighing 10 Kg., was fitted with a bronchovenous cannula. A small rubber bag connected with a rubber tube was introduced by bronchoscope into the primary bronchus on the side of the cannula. By inflating the bag suddenly during expiration, the bronchus was blocked and a negative pressure established in the peripheral bronchi in inspiration.

The bronchovenous cannula was released; no air passed into the vein. The bronchus block was released; fatal air embolism immediately took place.

A similar result was seen in the other dogs.

DEDUCTIONS

Spontaneous air embolism from an external fistula of the pulmonary vein was prevented in dogs by two means: (1) Positive pressure breathing (Tiegel), with pressure as low as 5 cm. of water; pressures above 14 cm. of water caused the vein to bleed. (2) The intravenous injection of epinephrine or ephedrine; the protection lasted only while the blood pressure remained above certain levels, which was only a few minutes. Accompanying this was a tendency to bleed from the vein.

Spontaneous embolism from a bronchovenous fistula in dogs was prevented by two means: (1) The intravenous injection of epinephrine or ephedrine; the effects were the same as in external fistula. (2) Bronchial block; protection lasted as long as the block was maintained, and without tendency to bleed from the vein. The use of positive pressure or negative pressure breathing afforded no protection but rather encouraged embolism.

TREATMENT

Consistent benefit in air embolism from the pulmonary vein has not been obtained experimentally or clinically by any form of treatment. Cardiorespiratory stimulants and intracardiac injections of epinephrine

have had no effect. Gundermann¹⁰ exposed the heart in dogs and aspirated and massaged the ventricle but could not rescue any one. He explained his failure by indicating the cause of heart failure as myocardial ischemia, necessarily resistant to any artificial stimulant short of reestablishment of the coronary circulation. Reyer and Kohl⁵⁰ suggested that the person's head be lowered after embolism, in order to bring additional blood to the brain, but this has not proved of assistance.

EXPERIMENTAL WORK

Two measures appeared of likely value in treatment, as indicated by the aforementioned experimental observations, i.e., artificial respiration and the use of the head-down position preliminary to air embolism.

Artificial Respiration, Seven Dogs.—These experiments were carried out in the following manner:

Each dog was placed under general anesthesia in the horizontal position, and a pulmonary vein cannula was inserted. Continuous intratracheal insufflation of air, according to the original principle of Meltzer and Auer,⁵¹ was instituted, and then a measured dose of air was injected into the pulmonary vein at a rate of 25 cc. per minute. The outcome was noted, whether by death or by recovery at four hours. The amounts of air were varied, to determine the maximum tolerance dose.

The maximum tolerance dose was 1.5 cc. per kilogram, which is the same as that found without artificial respiration in this position.

Vertical Position, Head Down, Thirty-two Dogs.—Experiments have been described in the section on tolerance (fig. 9) which indicate that, when the dog is in a vertical position, head down, the maximum tolerance dose is 3.3 cc. per kilogram of body weight, or two times that in the horizontal position.

Vertical Position, Head Down, Plus Artificial Respiration, Fifteen Dogs.—The artificial respiration was combined with the head-down position, described in the two previous experiments. The maximum tolerance dose for air injected into the pulmonary vein was found to be 5 cc. per kilogram of body weight or 50 per cent greater than with the head-down position alone.

This increased tolerance to air embolism was obtained only when artificial respiration was maintained at least one-half hour and when the position was held for one hour or more. The latter requirement is emphasized by experiment:

Dog 111, weighing 12 Kg., under general anesthesia, was placed in a head-down position and given 5 cc. of air per kilogram of body weight into the pulmonary vein, and the reaction was noted (fig. 12).

At thirty-eight minutes, recovery from the embolism seemed complete. The anesthetic had been discontinued and the dog had regained consciousness. The

50. Reyer, G. W., and Kohl, H. W.: Air Embolism Complicating Thoracic Surgery. J. A. M. A. **87**:1626 (Nov. 13) 1926.

51. Meltzer, S., and Auer, J.: J. Exper. Med. **11**:622, 1909.

table was lowered to the horizontal position. Immediately, the blood pressure rose slightly and then dropped steadily to 0 at forty-seven minutes.

At autopsy, it was found that air that had accumulated in the large trunk and the arteries of the hind legs had passed backward against the blood stream, ascended the aorta and reached the branches leading to the head and the coronary arteries. This retrograde embolism had obviously occurred at the time of change of the animal's position.

This occurrence of retrograde embolism on change of body position was demonstrated in two other dogs by means of air traps inserted in various vessels.

DEDUCTIONS

Treatment for air embolism from the pulmonary vein by artificial respiration (intratracheal insufflation of Meltzer and Auer) is of assistance only when the animal has been placed in a steep, head-down position before the onset of embolism. The tolerance for air embolus

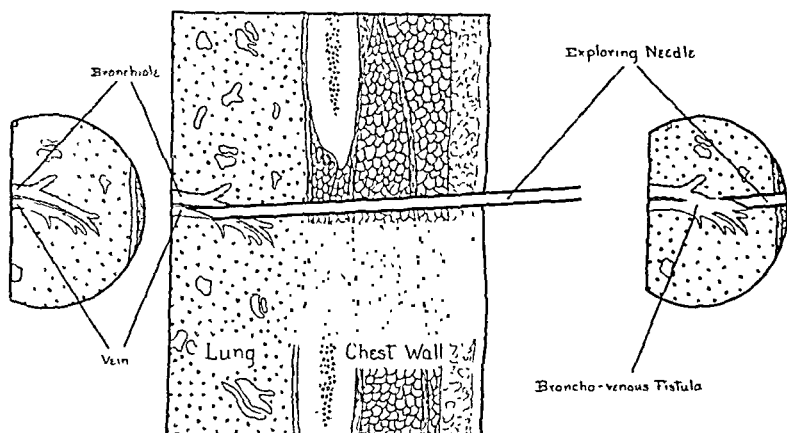


FIG. 13.—Cross-section of the thoracic wall and underlying lung with exploring needle in place. Illustrating the mode of formation of a bronchovenous fistula by needle puncture.

is then 5 cc. per kilogram of body weight, which is distinctly greater than under any other circumstances tested and is ten times as great as in the most susceptible circumstance, i.e., with the head up.

Artificial respiration must be continued for half an hour and the head-down posture for one hour in order to obtain the beneficial effects.

COMMENT

Air embolism from bronchovenous fistula is a complication demanding consideration in exploratory needle puncture of the lung, judging from the evidence of cases 1 and 2. In the parenchyma of the lungs the pulmonary veins lie in close proximity to bronchi, and transfixion of both vein and accompanying bronchus by the needle leaves defects in their walls at adjacent points (fig. 13). If, then, the parenchyma is

consolidated and inelastic, as it frequently is when such exploration is made, the pathway may remain temporarily patent. Likewise, a broncho-venous fistula may form readily in the case of a pulmonary cavity containing a vein in its wall, where a tangential needle thrust could tear the thin partition separating the lumen of the vein from the cavity. Given a patent bronchovenous communication, the vein becomes a branch of the bronchial tree and receives air during inspiration as voluminously as does any bronchial branch of like caliber. Here the person literally breathes into his circulation. The autopsy in case 1 revealed hundreds of cubic centimeters of air in the blood vessels. Such a mechanism may account for many of the obscure instances of sudden collapse following thoracotomy.

The extreme points of view commonly held as to the cause of these obscure complications following lung instrumentation, ascribing it entirely either to air embolism or to pleural reflex, are not justified by the available clinical and experimental evidence. That both entities exist as such and may occur in man and animals is established beyond reasonable doubt, as we have outlined, and differentiation must be made in diagnosing each case. Symptoms of irritation or paralysis of the higher brain centers point to embolism, but in the presence of cardiovascular symptoms alone either of the causes may be in play.

Differential diagnosis is assisted greatly by examination for one or both of two phenomena, i.e., sudden blood pressure alteration and "air bleeding." Marked depression of the blood pressure is seen in pleural reflex and other forms of shock, while elevation is characteristic of air embolism from the pulmonary veins. "Air bleeding" is, of course, pathognomonic of the latter. These signs are obtainable with instruments usually at hand and with no unusual amount of skill.

Air embolism from the pulmonary vein in its various forms is preventable. When there is a possibility of embolism occurring from external fistula of the vein, the use of positive pressure breathing may be relied on to eliminate the negative intrathoracic pressure and the capacity of the thoracic veins for suction. The Tiegel method (fig. 14) is perhaps the best, being simple and well tolerated by the conscious patient. Its principal advantage over other apparatus of the sort is the freely open breathing outlet, for submergence under water is used to procure pressure and there is no choking sensation produced as occurs with the spring valve devices, which elevate the pressure within the mask by obstruction to the outlet. Moreover, the water submersion principle sets the pressure desired and insures against accidental overdistention of the lungs. The pressure used is slight, from 8 to 10 cm. of water.

When there is a possibility of embolism from bronchovenous fistula, certain and controllable means of prevention are obtained only by

blocking the bronchus leading to the affected lung during the operation. The technic for this in man has not been developed but should be comparatively simple and without necessity of bronchoscopy. A fine catheter fitted at the end with a small rubber bag may be passed through the anesthetized larynx and into the bronchus under fluroscopic control, as in the Iglauer⁵² method for iodization. The use of epinephrine to raise the pulmonary intravenous pressure prevents spontaneous suction by the veins but the effect is too transient to be practicable.

The treatment for air embolism is of little avail. The embolized vital centers cannot be well reached by medication and there is no way of removing the air lodged in the vessels. Anoxemia may be prevented and distinct benefit obtained by the use of artificial respiration, as carried

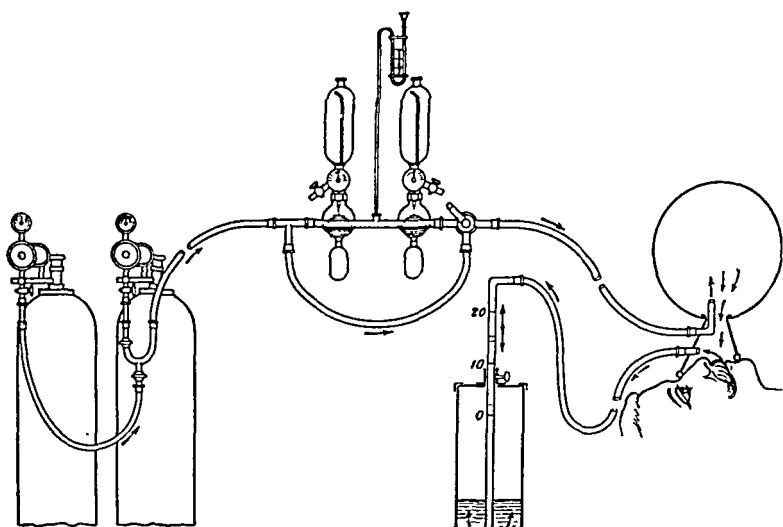


FIG. 14.—Positive pressure breathing apparatus applied to man, according to Tiegel. The air is supplied by tanks to the breathing mask and bag, and the exhaust air is carried out by a tube under water. The depth of the outlet under water determines the pressure breathed.

out in the experiments reported; this is not applicable to clinical experience, as only the principle of continuous intratracheal insufflation is desirable. Any procedure for administering artificial respiration which entails increasing the chest movements is likely to add to the air embolism and should be avoided. Once air embolism has occurred, it is of no benefit to institute the Trendelenberg position. The patient should be allowed to lie in the original position quietly and fight his own battle.

52. Iglauer, S.: Injected Iodized Oil in Roentgen-Ray Diagnoses of Laryngeal, Tracheal and Broncho-Pulmonary Conditions, *J. A. M. A.* **86**:1897 (June 19) 1926.

When an operation is contemplated in which there is a possibility of air embolism occurring and when certain means of prevention are not at hand the following procedure is advocated:

During the stage of the operation in which embolism is likely to occur, the patient is placed in a steep Trendelenberg position. The blood pressure is taken every minute or so, to warn of complications and indicate immediate interruption of the operation. If a sudden, marked elevation points to embolism, the diagnosis may be confirmed by eliciting "air bleeding," and the patient must then be maintained in the head-down posture for about two hours, to obviate shifting of the air to other parts of the body (coronary and cerebral vessels). Oxygen may be administered with a tent or other efficient passive methods.

SUMMARY

The subject of air embolism from the pulmonary vein is considered in this paper as to etiology, distribution of the air in the circulation, physiologic reaction, tolerance, cause of death, diagnosis, prognosis, prevention and treatment. Under each of these captions is given a review of the present knowledge and original clinical and experimental observations and deductions.

Particular emphasis is placed on the following conclusions:

1. Bronchovenous fistula may be produced by simple thoracentesis and may form a portal of entry for air into the pulmonary veins.
2. Gravity is a determining factor distributing air in the blood circulation.
3. Embolism of the heart (coronary) and brain are the vital effects. The position of the animal determines which of these are primary in a given case.
4. Tolerance for embolism is greatest when the head of the animal is well depressed and least with the head up.
5. Diagnosis is aided by two characteristic and easily elicited signs, i.e., elevation of the initial blood pressure and "air bleeding."
6. Prevention is certain by employing positive pressure breathing, when an external venous fistula is present, or by bronchial block, when a bronchovenous fistula exists.
7. Treatment, although effective under ideal circumstances, is not practical.

EXPERIMENTAL PEPTIC ULCER *

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REVIEW OF THE LITERATURE

A consideration of the numerous methods of procedure used in the experimental study of peptic ulcer shows that experimental ulcers may be grouped under a few general headings: (1) resulting from a deficient blood supply to the gastric mucosa; (2) produced by the action of bacteria; (3) resulting from the action of toxic agents; (4) resulting from trophic and glandular disturbances, and (5) produced by the action of the digestive juices.

Prior to Virchow's time, experimental studies of the problem had not been carried out. Indeed, a clear recognition of peptic ulcer as a distinct pathologic and clinical entity was not achieved until comparatively late in the progress of medical science. Galen, Celsus and other ancient investigators, presented vague and doubtful references to the ulcer in their descriptions of *passia cardiaca*, *hematemesis* and *melena*. The post-mortem examinations of the sixteenth century, stimulated by the general revival of original investigation, resulted in many descriptions of ulcer and cicatrices of the stomach. Bonetus (1679) published in the *Sepulchretum* one of the earliest recorded cases of perforating ulcer, which was observed by John Bauhin; other cases were described in the next century by Donatus, Courtial, Littre, Shenck and Morgagni. Matthew Baillie (1793) published the first accurate study of the anatomic peculiarities of ulcer; he republished the work later with three engravings and clinical data, but it had little influence on contemporary medical thought. A valuable description of the clinical syndrome, including nearly all the symptoms now recognized as characteristic of the malady, was published by John Abercrombie (1824). Cruveilhier (1829-1835) was the first to differentiate clearly ulcer of the stomach, carcinoma of the stomach and ordinary gastritis. He gave a clear anatomic and clinical description of the disease suggesting, as its primary cause, preceding gastritis. He anticipated the modern view expressed by Nauwerck¹ and supported by the studies of Konjetzny²

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* Abridgment of thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfilment of the degree of Doctor of Philosophy in Surgery.

1. Nauwerck, C.: *Mykotisch-peptisches Magengeschwür*, München. med. Wehnschr. **42**:876 and 908, 1895.

2. Konjetzny, G. E.: *Entzündliche Genese des Magen-Duodenalgeschwürs*, Arch. f. Verdauungskr. **36**:189, 1925.

and others, that gastritis might be the primary condition and the basis of the formation of ulcer. The other modern view, that hemorrhagic erosions establish the basis for a subsequent ulcerative process, was first expressed by Rokitansky³ in his description of seventy-nine cases.

VASCULAR SUPPLY

Historically, the first groping toward an explanation of the cause of ulcer was the concept of vascular insufficiency. Theory preceded experiment and outlined its development. Virchow⁴ announced his theory that vascular infarction was the primary etiologic factor in causing the formation of ulcer in the stomach. He visualized an ulcer as local ischemic necrosis induced by the embolic occlusion of a vessel; this vascular lesion mechanically removed the alkalinizing influence of the blood, and permitted the local destruction of the gastric wall by the corroding hydrochloric acid. The typical conical shape of the ulcer and its eccentric perforation of the serous coat depended, he believed, on the conical distribution of the tuft of vessels arising from the occluded eccentric arterial rootlet. Janeway⁵ presented to the New York Pathological Society a clinical case of ulcer with a fibrinous plug in a branch of the gastro-epiploic artery leading to the ulcer; a source of the plug was not found. Cohnheim,⁶ in reviewing the old authorities, recalled Klebs'⁷ belief that local ischemia due to spastic contraction of the arteries furnished the basis for ulceration; that Virchow attributed it to disease of the vessels, particularly embolic occlusion; that Günsburg⁷ thought impediments to the escape of venous blood acted as a cause; that Key⁷ held that mechanical hyperemia, caused by abnormal contraction of the gastric musculature, might cause local hemorrhage leading to the formation of the ulcer, and that Quincke believed general anemia to be a significant factor.

Embolus.—Experimental study of these hypotheses was first attempted by Panum⁸ and Cohnheim.⁶ Accepting Virchow's theory, Panum injected an emulsion of wax into the central end of the femoral artery of dogs; multiple small hemorrhagic infarcts and ulcers formed in

3. Rokitansky, Carl: A Manual of Pathological Anatomy, London, Sydenham Society, 1849, vol. 2, p. 31.

4. Virchow, R.: Historisches, kritisches und positives zur Lehre der Unterleibsaffektionen, Virchows Arch. f. path. Anat. 5:362, 1853.

5. Janeway, E. G.: The Cause of Perforating Ulcer of Stomach, M. Rec. 6:427, 1871-1872.

6. Cohnheim, J.: Lectures on General Pathology, London, The New Sydenham Society, 1890, vol. 3, p. 875.

7. Klebs; Günsburg, and Key, quoted by Cohnheim: Lectures on General Pathology, London, The New Sydenham Society, 1890.

8. Panum, P. L.: Experimentelle Beiträge zur Lehre von der Embolie, Virchows Arch. f. path. Anat. 25:433, 1862.

the stomach. However, the dogs died within twenty-four hours from widely disseminated emboli, so that the ultimate course of these ulcers was a matter of conjecture. Cohnheim injected lead chromate suspension into the gastric branches of the splenic artery, which caused large ulcers with precipitous walls on the second day; several small ulcers persisted into the second week, and complete healing occurred in the third week. In subsequent studies, Payr⁹ and Grossi¹⁰ injected a suspension of bismuth subgallate in sterile water into the gastric veins of twenty dogs, which caused submucous hemorrhage and acute ulcerations. Chessine and Feldmann,¹¹ injecting a 10 per cent emulsion of bismuth subgallate, produced infarcts of the mucosa, but only when they induced concurrent secondary anemia (hemoglobin 40 per cent) by the intravenous injection of chloral hydrate and phenylhydrazine; all ulcers were healed in thirty days, one showing cicatrization. Ivy¹² used finely divided emboli of animal charcoal, which gave negative results after injection into the gastro-epiploic vessels; however, using lead chromate and pigments, he produced ulcers which he interpreted as of toxic origin. Greggio¹³ and Bolton¹⁴ quoted other experiments on the injection of emboli which produced variable results: Sapiejko used lycopodium; Kobayashi and Nauverck used mycotic emboli; Vigliani used a "coagulating substance"; Rosenbach and Exner injected liquid paraffin and cultures of staphylococci into the gastro-epiploics; Shridde used fat emboli; Klebs and Welti used emboli formed from blood corpuscles and pigment granules, and Prevost and Cottard introduced tobacco into the aorta of a rabbit. Wilkie,¹⁵ interpreting the hematemeses that occasionally follows abdominal operations as due to retrograde emboli from omental thrombosis, injected solid particles of sterile oil into an omental vein. These particles impacting in the smaller venous branches caused submucous erosions and definite infarctions of the stomach, with associated infarcts of the spleen and liver. Greggio cited other studies, with the

9. Payr, Erwin: Experimente über Magenveränderungen als Folge von Thrombose und Embolie im Pfortadergebiete, *Arch. f. klin. Chir.* **84**:799, 1907.

10. Grossi, V.: Recherches expérimentales sur la production de l'ulcère gastrique par troubles circulatoires, *J. de chir.* **17**:502, 1921.

11. Chessine, V. R., and Feldmann, A. S.: Étude sur l'ulcère expérimental de l'estomac, *J. de chir.* **10**:65, 1913.

12. Ivy, A. C.: Studies on the Experimental Gastric and Duodenal Ulcer, *Am. J. Physiol.* **49**:143, 1919-1920; Contributions to the Physiology of the Stomach: LII. Studies on Gastric Ulcer, *Arch. Int. Med.* **25**:6 (Jan.) 1920; Studies on Gastric and Duodenal Ulcer, *J. A. M. A.* **75**:1540 (Dec. 4) 1920.

13. Greggio, Ettore: Des ulcères gastro-duodénaux, *Arch. de méd. expér. et d'anat. path.* **27**:533, 1916-1917.

14. Bolton, Charles: Ulcer of the Stomach, London, Edward Arnold, 1913, p. 386.

15. Wilkie, D. P. D.: Retrograde Venous Embolism as a Cause of Gastric Ulcer, *J. Path. & Bact.* **15**:355, 1911.

omentum: Sapiejko burned it, and Eiselberg, Friedlich, Pavy, Schiff, Matthes and Gibelli ligated it, all with uncertain or negative results.

Ligation of Vessels.—These unsatisfactory methods of study were supplanted by ligation of vessels. Littbauer¹⁶ found the anastomosis of vessels so free that a third of the blood supply to the stomach could be cut off without the formation of ulcer. Turck¹⁷ ligated all the vessels of the stomach and produced erosions. Fenwick¹⁸ failed to produce lesions by ligating only a few veins, but by tying most of them and injecting the portal vein with tincture of perchloride of iron, he produced hemorrhages and ulcers. Bolton quoted Mueller, Pavy, Roth and Litten as obtaining negative results from ligature of the larger arteries. Interference with the blood supply associated with injury to the mucosa was studied by Littbauer; he tied all the vessels in a given portion of the stomach, excised a piece of mucosa from that area and fed dilute hydrochloric acid; he procured ulcers in only two of eight experiments. Clairmont,¹⁹ Greggio²⁰ and Matthes²⁰ performed similar experiments, cauterizing the borders of the ulcer with hydrochloric acid, and found that ulcers formed easily in the pyloric region but not in the cardiac region. Yano²¹ found that whereas ligation of the gastro-epiploic arteries had no effect on the fundic mucosa, ligation of the gastric or pyloric artery led, as shown by intravenous injections of dye, to localized nutritional disturbances in the "Magenstrasse" of Waldeyer and Aschoff.

The studies on vascular occlusion in relation to the formation of ulcer suggested to Berlet²² a possible relationship between the anatomic distribution of the vessels and the site of greatest ulcer incidence. He injected the gastric arteries of twenty cadavers with a solution of gelatin containing red lead. Roentgen studies demonstrated that the blood

16. Littbauer, Max: Experimentelle Untersuchungen zur Pathogenese des runden Magengeschwürs, Arch. f. path. Anat. u. Physiol. **95**:317, 1909; Recherches expérimentales sur la pathogénie de l'ulcère rond stomacal, J. de chir. **2**:424, 1909.

17. Turck, F. B.: Preliminary Report on Ulcer of the Stomach: Pathogenesis and Pathology, Tr. Path. Soc. Chicago **6**:439, 1903-1906.

18. Fenwick, quoted by Bolton: Ulcer of the Stomach, London, Edward Arnold, 1913.

19. Clairmont, Paul: Ueber das experimentelle erzeugte Ulcus ventriculi und seine Heilung durch die Gastroenterostomie, Arch. f. klin. Chir. **86**:1, 1908.

20. Matthes, Max: Untersuchungen über die Pathogenese des Ulcus rotundum ventriculi und über den Einfluss von Verdauungsenzym auf lebendes und todes Gewebe, Beitr. z. path. Anat. **13**:309, 1893.

21. Yano, quoted by Aschoff: Lectures on Pathology, New York, Paul B. Hoeber Company, 1924.

22. Berlet, K.: Ueber die Arterien des menschlichen Magens und ihre Beziehungen zur Aetiologie und Pathogenese des Magengeschwürs, Frankfurt: Ztschr. f. Path. **30**:472, 1924.

supply to the pyloric region was much more sparse than that to the other parts of the stomach. He inferred that this predisposed the region to circulatory disturbances, rendering it much less capable of developing compensatory collateral circulation. Reeves²³ found that the vessels in the submucosa of the lesser curvature are smaller and longer, without as free anastomosis as in the other regions of the stomach; also that they are tortuous, with constantly increasing resistance to the blood stream. In the first part of the duodenum there are relatively few vessels in comparison with other parts of the duodenum. He concluded that these vessels are more prone to occlusion by emboli and may play an important part in the production of ulcer by hematogenous infection.

Occlusion of Vessels.—The theory sponsored by von Bergmann,²⁴ that spastic contraction of the arteries causes local ischemia which is the starting point for digestion by the gastric juice and subsequent ulceration, has met with considerable favor among German investigators. Westphal,²⁵ trying to prove the spasmogenic theory of Klebs and von Bergmann, injected large subcutaneous doses of pilocarpine, with and without physostigmine, into rabbits. This produced ulcers and erosions which he considered to be the result of spastic muscular contraction due to extreme vagal irritation. His experiments with cats, dogs and guinea-pigs were not so successful. With the stomach of the rabbit exposed, he observed long continued, spasmodically increased peristalsis, followed by cyanosis and pallor; snow-white specks appeared suddenly on the mucosa in which a dark center occurred. The anemic foci he believed to be due to vascular spasm with impoverishment of the blood supply to the mucosa. On the basis of the lesion ranging from hemorrhagic erosions to chronic perforating ulcers, which were produced with pilocarpine, epinephrine and morphine, singly and combined, Nakashima²⁶ accepted von Bergmann's theory as the most logical explanation of the pathogenesis of ulcer. Underhill and Freiheit²⁷ made direct observations on the stomach after injecting pilocarpine and epinephrine, from which they concluded that the lesions depended on cyanosis of the stomach and localized areas of anemia, on which the gastric contents exerted

23. Reeves, T. B.: A Study of the Arteries Supplying the Stomach and Duodenum and Their Relation to Ulcer, *Surg. Gynec. Obst.* **30**:374, 1920.

24. Von Bergmann, G.: *Ulcus-Probleme*, Jahresk. f. ärztl. Fortbild. **12**:3, 1921.

25. Westphal, K.: Untersuchungen zur Frage der nervösen Entstehung peptischer Ulcera, *Deutsches Arch. f. klin. Med.* **114**:327, 1914.

26. Nakashima, Yoshisada: Die Pathogenese des *Ulcus pepticum ventriculi et duodeni* experimentelle Beiträge zu von Bergmanns spasmogener Theorie, *Ztschr. f. d. ges. exper. Med.* **47**:4, 1925.

27. Underhill, F. D., and Freiheit, J. M.: Effect of Pilocarpine and Epinephrine in Production of Specific Lesions in the Stomach of Rabbits, *Arch. Path.* **5**:411 (March) 1928.

a destructive action. Hayashi²⁸ interpreted the ulcerous changes produced by injecting nicotine into guinea-pigs as due to obstruction of the arteries by muscular contraction. Gallagher²⁹ demonstrated that localized anemia of the duodenal mucosa produced by pressure, if it were maintained for a minimal period of forty minutes, resulted in superficial ulcers. Haeller³⁰ declared that Westphal's results were not due to gastric spasm, but to disturbances of the circulation and metabolism resulting from severe general intoxication. He believed the lesions to be a result of the toxic action of the drug, as he produced ulcerations with morphine, physostigmine and atropine, which exert a different physiologic effect.

Connor,³¹ in a histologic study of peptic ulcers, ascribed the chronicity of ulcer and its failure to heal to thrombosis of the vessels in the surrounding tissue. It is possible that this thrombosis is an effect and not the cause of the local condition, for Mann has reported a thrombotic process from the inflammatory reaction accompanying experimental ulcers. The fact that Morton³² procured healing of ulcers after gastro-enterostomy indicates that the thrombotic element, which would have been unaffected by this surgical procedure, might not have been the essential factor in maintaining chronicity. Konjetzny² did not observe thrombosis in the areas of gastritis and duodenitis, which he regarded as the possible basis of the formation of ulcer.

Anemia.—Many investigators have believed that general anemia as well as local vascular insufficiency has some bearing on the production of ulcer. Quincke first suggested this possibility. Zironi³³ produced ulcerations in 80 per cent of animals rendered anemic by the injection of pyrodine after bilateral vagotomy; in the absence of anemia, lesions appeared in only 59 per cent of cases and were neither so deep nor so extensive. Silbermann,³⁴ Litthauer¹⁶ and Matthes²⁰ presented evidence

28. Hayashi, Toshii: Experimentelle Beiträge zur Frage der Ulcusentstehung, Ztschr. f. d. ges. exper. Med. **34**:224, 1923.

29. Gallagher, W. J.: Acute Traumatic Ulcers of the Small Intestine, Arch. Surg. **15**:689 (Nov.) 1927.

30. Haeller, S. J.: Untersuchungen zur neurogenen Pathogenese des Ulcus ventriculi pepticum, München. med. Wchnschr. **1**:393, 1920.

31. Connor, C. L.: The Etiology and Pathology of Peptic Ulcer, Boston M. & S. J. **195**:971, 1926.

32. Morton, C. B.: Observations on Peptic Ulcer: I. A Method of Producing Chronic Gastric Ulcer: A Consideration of Etiology; II. A Röntgenologic Study of Experimental Chronic Ulcer; III. Healing of Experimental Peptic Ulcer After Gastro-Enterostomy, Ann. Surg. **85**:207, 1927.

33. Zironi, Giuseppe. Contributo sperimentale alla patogenesi dell' ulcera rotonda dello stomaco, Riforma med. **24**:1046, 1908; Experimenteller Beitrag zur Pathogenese des Ulcus rotundum des Magens, Arch. f. klin. Chir. **91**:662, 1910.

34. Silbermann, quoted by Bolton: Ulcer of the Stomach, London, Edward Arnold, 1913.

to show that anemia and hyperchlorhydria prolonged acute ulcers only to a negligible degree. Turck reported that ulcers occurred in animals simply by keeping them in close confinement until they were debilitated. Gibelli³⁵ reported negative results after anemia produced by bleeding.

Portal Insufficiency.—Finally, interference with the portal circulation, although of indirect action, has been associated with the formation of ulcer. Mueller³⁶ and Fenwick,¹⁸ by sudden occlusion of the portal vein, caused hemorrhages of the mucosa and ulcerations, chiefly in the cardiac end of the stomach. Following ligation of the portal vein, Gundermann³⁷ observed hepatic dysfunction with cerebral, renal and digestive disturbances; hemorrhages and ulcerations occurred in the stomach and duodenum. Payr produced acute ulcers (also certain chronic types) which perforated in three weeks by compression of the portal vein and injections of alcohol and formaldehyde. Turck interrupted the blood supply to the liver and ligated the blood vessels on the lesser curvature of the stomach; this resulted in congestion with hemorrhagic spots and erosions in the stomach. Bollman and Mann³⁸ reported that in a fairly large percentage of dogs subjected to true Eck fistula and fed with coarse kennel food perforating duodenal ulcers may form after a period of several months.

BACTERIAL RELATIONSHIP

As Virchow's theory of the vascular origin of ulcer had initiated considerable study of the influence of that factor, so Cruveilhier's comparison of peptic ulcer to intestinal typhoid ulcer stimulated investigation of the bacteriologic relationship of ulcer.

Early Experiments.—Lebert (1837), probably stimulated by the contemporary advances in bacteriology, injected pus into the veins of animals, with resulting pyemia and erosions of the gastric mucosa. Cohn (1860) produced similar erosions by the same method. The presence of bacteria in the marginal tissues of ulcer was demonstrated first by Böttcher (1874). Greggio and Bolton reviewed the earliest bacteriologic studies as follows: Lettule (1828) produced gastric lesions by the intravenous injection of *Bacillus pyocyaneus*; so also did Charrin and Ruffer. Wurtz and Leudet used lactic bacillus; Rosenbach and

35. Gibelli, D. C.: Contributo critico sperimentale all'esiologie dell' ulcera gastrica in rapporto coi traumi, Arch. internat. d. chir. 4:127, 1908.

36. Mueller, Ludwig: Das corrosive Geschwür im Magen und Darmkanal (Ulcus ventriculi perforans chronicum rotundum), und dessen Behandlung, Stuttgart, Ferdinand Enke, 1860, p. 274.

37. Gundermann, W.: Production expérimentale d'ulcères gastriques et duodénaux; contribution à l'étude d'une fonction pathologique du foie, J. de chir. 12:635, 1914.

38. Bollman, J. L., and Mann, F. C.: Chronic Duodenal Ulcer in Animals with Eck Fistulas on Certain Diets, Arch. Path. 4:492 (Sept.) 1927.

Eshker and Widal and Meslayo, the staphylococcus; Chantmesse and Widal, bacillus of dysentery; Bieulafoy, Bengancon and Griffen, pneumococcus; Saltineano, a coccobacillus and the bacillus of Pfeiffer; Favre, an organism from the blood of a patient with eclampsia, and Rodet and Zaidmann, *Bacillus coli*. The results of these studies were variable, usually with the production of certain gastric erosions.

Ingestion of Bacteria.—Subsequent investigators have adopted two definite methods: the introduction of bacteria by ingestion, or by intravenous injection. Sometimes concomitant procedures were adopted to enhance the action of the bacteria; for example, the production of an artificial anemia. Turck³⁹ produced both acute and chronic ulcers by feeding *Bacillus coli-communis* obtained from the feces of a patient with ulcer to a series of dogs over a long period of time; negative results were observed after the intravenous injection of the same organism. Singer⁴⁰ mixed excreta with the food and observed varying results, but never any lesions comparable to chronic ulcer. Ivy fed cultures of virulent streptococci, and at the same time produced lesions at the pylorus by pinching the mucosa. In five normal dogs the lacerations healed in from five to ten days; in five cachetic animals indurated ulcers occurred in from four to six weeks, and acid was absent in the stomach. He believed that with hypo-acidity swallowed bacteria were implanted in petechial hemorrhages or erosions, and, as a consequence, inflammation and induration of the edges, associated with a defective blood supply, delayed the regeneration of the mucous membrane. Although the general condition improved, chronicity persisted in the ulcer, due, he believed, to the diminished blood supply, the mechanical irritation by coarse foods, the tonic gastric activity and the action of acid pepsin on the devitalized tissue in the base of the ulcer. Rosenow⁴¹ could not demonstrate the formation of ulcer after the oral administration of

39. Turck, F. B.: Experiments in Producing Artificial Gastric Ulcer and Genuine Induced Peptic Ulcer, *J. A. M. A.* **46**:1753 (June 9) 1905; Further Observations on the Etiology and Pathology of Peptic Ulcer, *Brit. M. J.* **1**:922, 1907; Experimental Studies on Round Ulcer of the Stomach and Duodenum, *J. M. Research* **17**:365, 1907-1908.

40. Singer, quoted by Greggio: *Arch. de méd. expér. et d'anat. path.* **27**:533, 1916-1917.

41. Rosenow, E. C.: The Production of Ulcer of the Stomach by Injection of Streptococci, *J. A. M. A.* **61**:1947 (Nov. 29) 1913; Pathogenesis of Spontaneous and Experimental Appendicitis, Ulcer of Stomach and Cholecystitis, *J. Indiana M. A.* **8**:458, 1915; The Causation of Gastric and Duodenal Ulcer by Streptococci, *J. Infect. Dis.* **19**:333, 1916; Focal Infection and Elective Localization of Bacteria in Appendicitis, Ulcer of Stomach, Cholecystitis, and Pancreatitis, *Surg. Gynec. Obst.* **33**:19, 1921; The Etiology of Spontaneous Ulcer of the Stomach in Domestic Animals, *J. Infect. Dis.* **32**:384, 1923; The Specificity of the Streptococcus of Gastroduodenal Ulcer and Certain Factors Determining Its Localization, *ibid.* **33**:248, 1923. Rosenow, E. C., and Sanford, A. H.: The Bacteriology of Ulcer of the Stomach and Duodenum in Man, *J. Infect. Dis.* **17**:219, 1915.

streptococcic strains which produced lesions by intravenous injection, even after the admixture of sharp particles to the diet. Wilensky and Geist⁴² isolated streptococci according to Rosenow's technic, excised a piece of gastric mucosa and injected the organism into the defect at the time of operation. The injection was repeated subsequently when it tended to heal. The characteristics of chronic induration failed to develop in any ulcer and healing was not retarded.

Kotzareff and de Morsier,⁴³ continuing the work of Askanazy⁴⁴ and Kotzareff, injected *Oidium albicans* into local defects in the gastric mucosa of dogs, pigs, guinea-pigs and rabbits. They began their injections twenty-four hours after scraping the mucosa from the lesser curvature and the pylorus, and continued them daily for twenty days. The animals died with acute gastritis, or with perforated or chronic perforating ulcer, and the organism was recovered from the lesion.

Injection of Bacteria.—More definite and constant results have followed the injection of organisms into the blood stream. Steinharter⁴⁵ reported the production of gastric and duodenal ulcers following the intravenous injection of a staphylococcus isolated from an acutely inflamed appendix; the ulcers varied in size from 1 to 7 mm. and were cleanly punched out and circumscribed. Previously, he reported⁴⁶ the production of acute superficial ulcer following the injection of *Bacillus coli-communis* into the vein of an ear of a rabbit; also after the injection of *Staphylococcus pyogenes* into the wall of the stomach with the simultaneous administration of weak acetic acid by mouth. Hoffman⁴⁷ claimed that he isolated a comma-shaped bacillus from the gastric contents in a case of ulcer which, on intraperitoneal injection into a guinea-pig, produced lesions of the stomach and duodenum with duodenitis. The organism was recovered and cultivated, and the lesion was reproduced on second animal passage, thus conforming to Koch's laws.

42. Wilensky, A. O., and Geist, S. H.: Experimental Studies in the Production of Chronic Gastric Ulcer, *J. A. M. A.* **66**:1382 (April 29) 1916.

43. Kotzareff, A., and de Morsier, J.: Étiologie et pathogénie de l'ulcère chronique de l'estomac. Travail expérimental, *Zentralbl. f. Chir.* **52**:1404 1925.

44. Askanazy, M.: Ueber Bau und Entstehung des chronischen Magengeschwürs, sowie Scorpilzbefunde in ihm, *Virchows Arch. f. path. Anat.* **234**:111, 1921.

45. Steinharter, E. C.: Gastric Ulcer Experimentally Produced by Means of the Staphylococcus Organism: A Preliminary Note, *Boston M. & S. J.* **174**:678, 1916.

46. Steinharter, E. C.: A Preliminary Note on the Experimental Production of Gastric Ulcers by the Intravenous Injection of Clumped Colon Bacilli, *Boston M. & S. J.* **169**:81, 1913; Gastric Ulcer Produced by the Intravenous Injection of Staphylococcus Pyogenes, *ibid.* **176**:461, 1917.

47. Hoffman, A.: Experimental Gastric and Duodenal Inflammation and Ulcer, Produced with a Specific Organism Fulfilling Koch's Postulates, *Am. J. M. Sc.* **170**:212, 1925.

Hoffman believed it to be a specific organism with selective affinity for the stomach and duodenum. Kobayashi ⁴⁸ tied the cecum of a dog so that the peritoneum would become inflamed, and thus produced ulcers. Saïtta ⁴⁹ associated vagotomy or trauma with the injection of bacteria, but with varying results. Having observed that the injection of diphtheria toxin had produced erosions in the stomach, Rosenau and Anderson ⁵⁰ injected washed diphtheria bacilli into guinea-pigs, with resulting congestion, hemorrhage or ulceration near the pylorus. Hardt ⁵¹ was able to produce lesions following the injection of *Bacillus coli* in only four of eighteen cases (22 per cent), but following the injection of streptococci the ulcer incidence was 57 per cent; seven of these occurred in eight dogs with a Pavlov pouch, many in the pouch itself. This he claimed eliminated the mechanical and acid factors in the production of ulcer.

Specific Streptococci.—Recent studies have been directed toward determining the relationship of streptococci to the formation of ulcer. Ivy injected streptococci into branches of the gastro-epiploic vessels, causing dense fibrinous and fibrous perigastritis, but not ulceration. He concluded that a markedly virulent or specific bacterium is necessary to produce gastric ulceration. Celler and Thalhimer ⁵² recovered a hemolytic streptococcus from gastric ulcers, which, when injected intravenously into rabbits, caused gastric lesions in 13.3 per cent; when this substance was injected into a branch of the gastric artery, lesions were observed in 75 per cent of the cases. *Saccharomyces* and a gram-negative bacillus were also isolated with the streptococcus. From seventeen cases of chronic gastritis or duodenal ulcer, Haden and Bohan ⁵³ isolated a streptococcus which on injection showed gastric and duodenal lesions in 53 per cent of forty-five rabbits. As controls, streptococci from patients not having ulcers were injected into 535 rabbits, and gastric and duodenal lesions resulted in only 7 per cent.

The outstanding contribution on the relationship of streptococci to the formation of ulcer has been Rosenow's work ⁴¹ relating to the elec-

48. Kobayashi, quoted by Greggio: Arch. de méd. expér. et d'anat. path. **27**: 533, 1916-1917.

49. Saïtta, S.: Contributo alla patogenesi dell' ulcera gastrica, Gazz. d. osp. **21**:599, 1900.

50. Rosenau, M. J., and Anderson, J. F.: A Stomach Lesion in Guinea-Pigs Caused by Diphtheria Toxin and Its Bearing upon Experimental Gastric Ulcer, J. Infect. Dis. **4**:1, 1907.

51. Hardt, L. L.: Contributions to the Physiology of the Stomach: XXXIII. The Secretion of Gastric Juice in Cases of Gastric and Duodenal Ulcers, Am. J. Physiol. **40**:314, 1916.

52. Celler, H. L., and Thalhimer, William: Bacteriological and Experimental Studies on Gastric Ulcer, J. Exper. Med. **23**:791, 1916.

53. Haden, R. L., and Bohan, P. T.: Focal Infection in Peptic Ulcer, J. A. M. A. **84**:409 (Feb. 7) 1925.

tive localization of streptococci. He postulated that to prove the relationship of a specific strain of streptococcus to ulcer, it is necessary to demonstrate the organism in the ulcer, and to prove by injection that it can reproduce the lesion. He reported histologic studies of a series of ulcers and of their regional lymph nodes, in which streptococci were demonstrated, always most numerous where there was leukocytic infiltration of the subperitoneum. Using dextrose-brain broth, which supplied a gradient of oxygen tension, he cultivated the organisms isolated from ulcers, and from foci of infection in patients with ulcer. His theory is that by sojourn in the body in a focus, these streptococci acquire a specificity by virtue of which they are capable of elective localization in special tissues. To prove this he injected these specific strains of streptococci into rabbits. Hemorrhagic erosions and ulcerations resulted in 61 per cent of rabbits injected with ulcer strains, and in 28 per cent of those injected with strains from foci of the patients with ulcer. The incidence of ulcer was materially reduced by preliminary treatment with vaccine. Careful studies of joints, heart, nerves and other organs showed associated lesions in very low percentages. For a control study he injected nonspecific strains of streptococci into rabbits; gastric hemorrhage resulted in only 20 per cent of cases, and ulcer in only 9 per cent. The specific organisms lodge primarily in the interstitial tissue of the glands; hemorrhage, necrosis and ulceration follow.

Rosenow stated that the lesions resemble ulcers of patients, in situation and in gross and microscopic appearance, tending to become chronic and to perforate and cause fatal hemorrhage. The virulence of the specific strains is low, as death does not follow intraperitoneal injection into mice; nonspecific strains cause a mortality rate of 91 per cent. After cultivation on artificial mediums or after animal passage, the capacity for elective localization is retained only in 30 per cent of cases, and the organisms tend to shift, for example, from the stomach to the appendix or the gallbladder. Rosenow considers these organisms specific because of their apparent constant occurrence in the depths of ulcers of patients, to the exclusion of other organisms, and because they tend to localize in the stomach and duodenum of animals into which injections have been made, a property which is not exhibited by other organisms.

Haden,⁵⁴ Nickel and Hufford⁵⁵ and Nakamura⁵⁶ have done considerable work corroborating Rosenow's results. Using the technic described, Haden studied twelve cases of peptic ulcer from the stand-

54. Haden, R. L.: The Elective Localization of Bacteria in Peptic Ulcer, *Arch. Int. Med.* **35**:457 (April) 1925.

55. Nickel, A. C., and Hufford, A. R.: Elective Localization of Streptococci Isolated from Cases of Peptic Ulcer, *Arch. Int. Med.* **41**:210 (Feb.) 1928.

56. Nakamura, T.: A Study on Focal Infection and Elective Localization in Ulcer of the Stomach and in Arthritis, *Ann. Surg.* **79**:29, 1924.

point of dental infection. With cultures of streptococci obtained from diseased teeth extracted from patients with ulcer, he produced lesions of the stomach and duodenum in 53 per cent of forty-five rabbits which had received intravenous injections. Nakamura, in studying the dependence of symptoms of ulcer on foci of infection, noted that in nine patients the symptoms (including hemorrhage) were relieved by removal of the foci. In 70 per cent of sixty-six rabbits that received injections of the organisms from these foci, hemorrhagic erosions or ulcers were found near the pylorus; a low percentage of lesions was found in other organs. He emphasized the importance of foci of infection rather than of suture material in causing recurrence of ulcer at the line of anastomosis. Nickel and Hufford found a definite infective focus in all but one of eighty cases of duodenal ulcer; from these they isolated green-producing streptococci which produced lesions in the stomach and duodenum of rabbits when injected intravenously. Moody⁵⁷ studied the pathogenicity of *Streptococcus viridans* recovered from chronic alveolar abscesses in persons with rheumatism, in those with various different systemic disorders and in those perfectly well otherwise. In all the groups the percentage of localization in the stomach was high. He concluded that the lesions produced by organisms from persons without systemic disease are identical with those produced by organisms from persons with systemic disease. He admitted, however, the possibility of well persons later developing systemic disease from such foci. He stated, "There is evidence for and against the property of elective affinity of streptococci, but it cannot be determined wholly by some property inherent in the organism itself." Meisser⁵⁸ produced chronic foci in dogs by devitalizing four cuspids and injecting specific streptococci into the canals. He found hemorrhages or ulcerations or both in the stomach and duodenum of 65 per cent of the series of dogs.

Mention should be made here of the theory of inflammatory ulcer, based on the histologic studies of stomachs that have been resected for ulcer. These studies, although not experimental, have been carried out chiefly by Konjetzny,² Moszkowicz,⁶⁰ Orator,⁶⁰ Lehmann⁶¹ and Puhl.⁶²

57. Moody, A. M.: Lesions in Rabbits Produced by Streptococci from Chronic Alveolar Abscesses, *J. Infect. Dis.* **19**:515, 1916.

58. Meisser, J. G.: Further Studies on Elective Localization of Bacteria from Infected Teeth, *J. Am. Dent. A.* **12**:554, 1925.

59. Moszkowicz, Ludwig: Zur Histologie des Ulcus bereiten Magens, *Arch. f. klin. Chir.* **122**:444, 1922.

60. Orator, V.: Ueber die funktionelle Bedeutung der Magenstrasse und die cardianahen Geschwüre, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **36**:725, 1923.

61. Lehmann, J. C.: Neuere Anschauungen über die Pathogenese des Magenulcus und Karzinomas, *München. med. Wchnschr.* **1**:410, 1925.

62. Puhl, Hugo: Ueber die Bedeutung entzündlicher Prozesse für die Entstehung des Ulcus ventriculi et duodeni, *Virchows Arch. f. path. Anat.* **260**:1, 1926.

Because of the investigation of thousands of resected stomachs, these authors believe that in most cases of gastric or duodenal ulcer there exists gastritis or duodenitis. Puhl reported a series of cases in which the specimens were fixed immediately after removal. Abundant leukocytic infiltration, congestion and edema of the antrum, with ulcerations so numerous as to be called ulcerous gastritis, were found on histologic study. This inflammatory gastritis and duodenitis, with the accompanying superficial erosions, establish, according to this investigator, the necessary initial lesion for the subsequent development of chronic gastric ulcer. He observed gram-positive diplococci in the tissues, but since he was unable to culture them, he did not draw conclusions as to their significance.

TOXIC MANIFESTATIONS

The idea that a local injury to the gastric mucosa acts as the initial cause of ulceration has led to an extensive study of the effects of drugs and physical agents in causing ulceration of the mucosa of the stomach. These have been administered both systematically and locally. Bolton¹⁴ reviewed the work of early investigators who sought to produce lesions by the systemic action of drugs. Overbach rubbed gray ointment into the skin for a period of three months; von Mering injected glycocholate of mercury into cats and dogs; Pillet and Cathetineau used perchloride of mercury; Filhene used arsenious acid. Greggio's review added the work of Virchow and Ebstein, who used phosphorus poisoning; Brouardel and Böhm, who injected arsenious acid subcutaneously; Majer, d'Auitolo and Coen, who caused progressive poisoning of rabbits and dogs with lead acetate; Sarkowsky and Heilborn, who injected corrosive sublimate subcutaneously into rabbits; Ebstein and Peron, who used alcohol; Aufrecht, who used cantharides, and Roy and Poncet, who used ergot and digitalis.

Rehfuss⁶³ studied the effect of the subcutaneous injection of pilocarpine. Injections into guinea-pigs caused ulcer and hemorrhagic erosions in 85 per cent of cases; the effect of the drug was aggravated by the simultaneous administration of atropine. Haden has shown that industrial poisoning, as by benzene (C_6H_6), may cause lesions in the duodenum. Friedman,⁶⁴ by repeated injections of epinephrine for a period of from one to two weeks, produced duodenal ulceration. He also noted that after injections of pilocarpine the preponderance of lesions was in the gastric mucosa. Elliott⁶⁵ caused acute gastric ulcers by

63. Rehfuss, M.: The Experimental Production of Acute Toxic Ulcer of the Stomach, Univ. Penn. M. Bull. **22**:105, 1909-1910.

64. Friedman, G. A.: The Experimental Production of Lesions, Erosions and Acute Ulcers in Rabbits, by Repeated Injections of Pilocarpin and Adrenalin, J. M. Research **38**:449, 1918.

65. Elliott, T. R.: The Experimental Formation of Acute Gastric Ulcers, Quart. J. Med. **7**:119, 1914.

injecting tetrahydro-B-naphthylamine hydrochloride subcutaneously into a guinea-pig. The lesions formed within one or two hours if the stomach was kept filled with food; they were healed and covered with epithelium in three days, the glands regenerating later. Westphal, as has been noted, administered to rabbits large cutaneous doses of pilocarpine, either alone or combined with physostigmine, with resulting ulcers and erosions. He believed that these lesions resulted from vascular spasm due to extreme vagal irritation. In 1917, Murata⁶⁶ repeated these studies with the same results, but he ascribed the local ischemia to obstruction of the supplying artery by a spasmodic contraction of the gastric musculature. In the same year, Hayashi⁶⁷ produced ulcerous changes following the subcutaneous injection of nicotine into guinea-pigs. Later, Hayashi²⁸ caused similar lesions in rats with muscarine; he attributed the result to the elective action of this poison on the stomach by peripheral vagal irritation. The use of morphine, physostigmine, epinephrine and atropine has been mentioned.

Submucous Injection.—The effect of toxic agents when injected directly into the gastric wall has been thoroughly investigated. Greggio in his review stated that Borszéký and Baron produced ulcers by injecting formaldehyde into the gastric mucosa; Rosenbach and Eschker used epinephrine; Serzuki, Payr and Vigliani injected alcohol and chloral; Serzuki used epinephrine, silver nitrate and formaldehyde; Licini,⁶⁸ after injecting apomorphine into the musculature of the stomach, noted hypermotility which changed acute to chronic lesions. Greggio himself produced gastritis with injections of alcohol, but could not induce ulcer to form. Turck sought to produce ulcerous changes by feeding mustard over a period of fourteen months, but with negative results. Ivy produced lesions by injecting 1 cc. of 5 per cent silver nitrate into the submucosa. Friedman and Hamburger⁶⁹ used the same procedure associated with partial pyloric stenosis; hyperacidity resulted, ulcers near the pylorus became chronic, and those in the cardia tended to heal. Acute ulcers, which Dragstedt and Vaughan⁷⁰ observed after injecting silver nitrate, persisted for from three to four months and tended to

66. Murata, quoted by Hayashi: *Ztschr. f. d. ges. exper. Med.* **34**:224, 1923.

67. Hayashi (footnote 28, page 227). 605

68. Licini, Cesare: *Ueber experimentelle Erzeugung von Magenschwüren*, Beitr. z. klin. Chir. **79**:462, 1912.

69. Friedman, J. C., and Hamburger, W. W.: *Experimental Chronic Gastric Ulcer: A Second Contribution to the Experimental Pathology of the Stomach*, J. A. M. A. **63**:380 (Aug. 1) 1914.

70. Dragstedt, L. R., and Vaughan, A. M.: *Gastric Ulcer Studies. The Resistance of Various Tissue to Gastric Digestion*, Arch. Surg. **8**:791 (May) 1924. Dragstedt, L. R.: *Contributions to the Physiology of the Stomach: XXXVIII. Gastric Juice in Duodenal and Gastric Ulcers*, J. A. M. A. **68**:330 (March 17) 1917.

become chronic when loops of nonabsorbable suture material were embedded in the gastric walls at the points of injury. Similar ulcers were observed by Hughson⁷¹ to remain active twice as long when associated with delayed emptying of the stomach.

Biologic Toxins.—Of greater interest are those biologic products which exert a toxic action on the gastric mucosa. Ponfick⁷² observed clinical lesions of the stomach and duodenum, following superficial burns, in as short a time as eighteen hours, with associated congestion of the mucous membrane and enlarged lymphoid follicles. Silbermann,³⁴ Vassale and Sacchi⁷³ and Parrascandola caused ulcers in animals following large cutaneous burns, or by injecting the extracts of burned tissues. Greggio quoted Stoknis, Long, Sokoloff and Castel as having caused lesions by glazing the surface of the skin.

Bolton¹⁴ produced what he called a gastrototoxic serum (and an analogous hepatotoxin and enterotoxin) by injecting a suspension of gastric mucosa from a guinea-pig into the peritoneal cavity of a rabbit. After antibodies to this foreign protein had developed sufficient to establish the rabbit's immunity to it, an injection of this immune serum into the peritoneal cavity of a guinea-pig caused death, associated with lesions of the stomach. Injection of this toxin directly into the gastric mucosa also caused ulceration. Bolton found that although ordinarily hydrochloric acid does not exercise any effect on the gastric mucous membrane in concentrations below 0.7 per cent, yet any concentration from 0.25 to 0.7 per cent caused an increase in the size of the lesion produced by injecting gastrototoxic serum, and 0.5 per cent acetic acid (usually innocuous below 2 per cent) increased a lesion produced by the injection of gastrototoxin. Miyagawa, Murai and Terada,⁷⁴ adopting the same method, produced an homologous toxic serum. They immunized one rabbit to the gastric mucosa of another rabbit, and injected the serum of this immune rabbit locally into the gastric mucosa of a third rabbit. The interpretation of the production of these ulcers was that the reabsorption of toxic substances from the necrosed tissue of an ulcer leads to the production in the organism of a cytotoxin which prolongs ulcer and leads to chronicity. Hepatotoxin and enterotoxin, produced similarly

71. Hughson, W.: Relation of the Pylorus to Duration of Experimental Gastric Ulcer, *Arch. Surg.* **15**:66 (July) 1927.

72. Ponfick, quoted by Bolton: *Ulcer of the Stomach*, London, Edward Arnold, 1913.

73. Vassale, G., and Sacchi, E.: *Sulla tossicità dei tessuti scottati*, *Riforma med.* **9**:544, 1893.

74. Miyagawa, Yoneji; Murai, Hatsu, and Terada, Masachika: An Experimental Study of the Cells of the Mucous Membrane of the Digestive Tract as Toxin or Irritant, and Its Relation to the Formation of Peptic Ulcer, *Japan M. World* **3**:123, 1923.

from hepatic and intestinal tissues, were not so certain in their action as gastrotoxin, nor were they specific for a single species.

Latzel⁷⁵ sterilized the gastric juice of a guinea-pig, and by subcutaneous injections into other animals caused anaphylaxis and ulceration of the stomach. Jona⁷⁶ caused similar changes and inhibited pancreatic secretion by subcutaneous doses of extracts of decomposing animal tissues. Greggio, quoting the older workers who used biologic toxins, said that Loepez caused ulcerous changes by injecting a watery maceration of the mucosa or gastric juice of swine; Gundermann³⁷ caused it with extract of liver; Stick, with ptomaines, and Favre, with the blood of a uremic person. In corroboration of the work of Enriquez and Hallion (quoted by Bolton), Rosenau and Anderson⁵⁰ found that diphtheria toxin, when injected into guinea-pigs, caused hemorrhage and necrotic patches in the gastric mucosa. They found lesions in 66 per cent of guinea-pigs used in the production of antitoxin. If, however, the toxin was neutralized by antitoxin, a lesion did not appear. Necropsy revealed congestion, hemorrhage or ulceration at the pyloric extremity, associated with congested suprarenal glands and pleural effusion. Such results were not obtained with tetanus toxin or chemical poisons.

As an extension of his work on the elective localization of streptococci, Rosenow showed that the dead bacteria, or a filtrate of the living culture, possessed the same local affinity as the living organism, causing lesions in the stomach and duodenum. Ivy and Shapiro⁷⁷ injected foreign protein (albumin of egg, beef and cat protein) into the skin of a rabbit until a superficial ulcer formed from local anaphylaxis; this specific protein when later injected into the gastric mucosa caused ulcer to form.

Miscellaneous Methods.—Decker⁷⁸ produced erosions and ulcers by feeding dogs with gruel heated to 50 C. He attributed this not to the scalding but to the congestion of the mucous membrane and the hemor-

75. Latzel, R.: Recherches expérimentale sur l'étiologie de l'ulcère de l'estomac et conséquences théoriques sur la pathogénie de l'ulcère de l'estomac et du duodénum, *J. de chir.* **11**:788, 1913.

76. Jona, J. L.: An Experimental Study of Duodenal Ulcer, *M. J. Australia* **1**:165, 1918; A Further Contribution to the Experimental Study of Duodenal Ulcer, *ibid.* **1**:316, 1919; Experimental Study of Duodenal Ulcer, *Physiol. Abstr.* **4**:412, 1919.

77. Ivy, A. C., and Shapiro, P. F.: Studies on Gastric Ulcer: III. The Experimental Production of Gastric Ulcer by Local Allergy; Preliminary Report, *J. A. M. A.* **85**:1131 (Oct. 10) 1925. Shapiro, P. F., and Ivy, A. C.: Gastric Ulcer: IV. Experimental Production of Gastric Ulcer by Local Anaphylaxis, *Arch. Int. Med.* **38**:237 (Aug.) 1926.

78. Decker, J.: Experimentelle Beitrag zur Aëtiologie der Magengeschwüre, *Berl. klin. Wchnschr.* **24**:369, 1887.

rhagic erosions from increased peristalsis. Katzenstein⁷⁹ introduced small, hot, porcelain tubes into the stomach to burn the mucosa; this was followed by injection of phosphoric acid to destroy antipepsin and allow digestion. Ribbert⁸⁰ froze an area, 2 cm. in diameter, of the wall of the stomach with ethyl chloride and methethyl for twelve minutes. The following day a defect appeared in the gastric mucosa, which developed subsequently into an ulcer. Wolfer⁸¹ opened the anterior wall of the stomach, delivered the posterior wall and sutured a lead plate with a small opening to the mucosa. Through this small opening he exposed the mucosa to the roentgen rays and produced a round or oval ulcer with indurated raised margins. One of these ulcers persisted for 585 days. In a later study he noted that if such ulcers were produced close to the pylorus there was a definite delay in the emptying time of the stomach, but if farther away than 5 cm. there was no delay.

Rassers⁸² eliminated all chlorides from the diet of a series of dogs, and administered twelve, eighteen, twenty and twenty-four doses of strong acid pepsin solution over a period of from one to three days. He observed hemorrhagic erosions and small ulcerations in the pyloric antrum and duodenum, which he attributed to the failure of the cells to produce a protective hydroxide against the acid pepsin which was administered.

Kirch and Stahnke,⁸³ observing that in chronic ulcers the muscularis propia is always absent, produced mucosal defects in the stomachs of a series of dogs, and cut away the underlying muscle. From their results they concluded that destruction of the muscle delays healing and is an important factor in the chronicity of lesions, although it does not prevent healing. Morton,⁸² however, noted that healing took place with almost as great ease and rapidity when the muscularis was excised as when the mucosa alone was excised.

Baggio⁸⁴ folded in the anterior wall of the stomach and observed lesions ranging from simple erosions to typical advanced gastric ulcers

79. Katzenstein, M.: *Der Schutz des Magens gegen die Selbstverdauung nebst einem Vorschlag zur Behandlung des Ulcus ventriculi*, Berl. klin. Wchnschr. **45**: 1749, 1908. Quoted by Smith: *J. M. Research* **30**:147, 1914.

80. Ribbert, H.: *Experimentelle Magengeschwüre*, Frankfurt. Ztschr. f. Path. **16**:343, 1915.

81. Wolfer, J. A.: *Chronic Ulcer of the Stomach: Its Experimental Production and Effect on Gastric Secretion and Motility*, Ann. Surg. **84**:89, 1926; *Chronic Experimental Ulcer of the Stomach: Its Clinical Significance*, J. A. M. A. **87**:725 (Sept. 4) 1926.

82. Rassers, J. R. F.: *The Pathogenesis of Chronic Gastro-Intestinal Ulcer and Some Remarks on the Question of a Rational Therapy*, Surg. Gynec. Obst. **45**:345, 1927.

83. Kirch, E., and Stahnke, E.: *Delayed Healing of Chronic Gastric Ulcer from Destruction of Muscle*, Frankfurt. Ztschr. f. Path. **33**:269, 1925-1926.

84. Baggio, G.: *Experimental Gastric Ulcer from Obstruction to the Emptying of the Stomach*, Surg. Gynec. Obst. **44**:490, 1927.

on both the introflexion and the posterior wall opposite the introflexion. He attributed these lesions to the traumatic action of the ingesta and the obstruction caused by the introflexion. Slocumb⁸⁵ noted inflammatory changes and multiple ulcers in the duodenum of dogs in which he established partial obstruction of the duodenum by surgical measures.

Ivy noted five ulcers in forty dogs subjected to pylorotomy and gastroduodenostomy. Borszéký⁸⁶ narrowed the pylorus and performed gastro-enterostomy on twelve dogs; he fed them 30 cc. of dilute hydrochloric acid daily. Jejunal ulcers formed only in one of twelve dogs. Dott and Lim⁸⁷ claimed that they observed jejunal ulcers in 90 per cent of the dogs on which they performed pyloric exclusion and gastro-jejunosomy. Montgomery⁸⁸ found chronic jejunal ulcers in four of sixty dogs on which gastro-enterostomy had been performed. Exalto⁸⁹ performed gastro-enterostomy after excluding the pylorus; he then drained the duodenal alkalis of the proximal loop into the cecum. He observed jejunal ulcer, often multiple, in six of ten dogs operated on in this manner.

TROPHIC AND GLANDULAR ULCERS

A different conception of ulcer formation has directed the great volume of work accomplished by the Italian school. They interpret the lesion as of a neurotrophic order, dependent on a defect in the nerve supply to the stomach. Their researches have dealt chiefly with the influence of the vagi, although they have also investigated the central nervous system and splanchnic nerves.

Central Nervous System.—Ebstein⁹⁰ and Brown-Séquard,⁹¹ in the earliest studies on the central nervous system, obtained partial softening, erosion and formation of ulcer in the stomach following circumscribed destruction of the anterior corpora quadrigemina, and after burns of the

85. Slocumb, L. H.: Experimental Gastroduodenal Ulcer Produced by Partial Obstruction of Duodenum, *J. Missouri M. A.* **24**:351, 1927.

86. Borszéký, Karl: Die chirurgische Behandlung des peptischen Magen und Duodenalgeschwürs und seiner Komplikationen und die damit erreichten Endresultate, *Beitr. z. klin. Chir.* **57**:56, 1908.

87. Dott, N. M., and Lim, R. K. S.: Experimental Jejunal Ulcer, *Quart. J. Exper. Physiol., Suppl.*, 1923, p. 109.

88. Montgomery, A. H.: Gastrojejunal Ulcer: An Experimental Study, *Arch. Surg.* **6**:136 (Jan.) 1923.

89. Exalto, J.: Ulcus jejuni nach Gastroenterostomie, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **23**:13, 1911.

90. Ebstein, Wilhelm: Experimentelle Untersuchungen über das Zustandekommen von Blutextravasaten in der Magenschleimhaut, *Arch. f. exper. Path. u. Pharmakol.* **2**:183, 1874.

91. Brown-Séquard, quoted by Greggio: *Arch. de méd. expér. et d'anat. path.* **27**:533, 1916-1917. Quoted by Zironi: *Arch. f. klin. Chir.* **91**:662, 1910.

cerebral surfaces. Schiff⁹² observed hemorrhagic infiltrations and ulcerations following intersection of the thalamus and cerebral peduncles. Greggio noted mucosal and submucous hemorrhages near the pylorus,⁹³ associated with diffuse gastritis, in half of fifty cases subjected to unilateral and median compression of the cervical cord. He and Bolton cited the production of ulcer by Albertoni, who cut off the cerebral hemisphere; Ewald and Koch, who severed the cervical cord and administered 0.5 per cent hydrochloric acid daily; Schupfer, following bilateral lesions of the anterior and posterior roots of the fifth and eighth dorsal segments; and Quincke and Dättwyler,⁹⁴ who associated lesions of the cord with anemia.

Splanchnic Nerves.—While Durante⁹⁴ was studying the relationship of the splanchnic or sympathetic nerves to ulcerous changes, he repeated the work of Dalla Vedova.⁹⁵ He resected the splanchnic nerves by a lumbar approach, and found that section of the median splanchnic nerve produced circumscribed hemorrhagic or nonhemorrhagic necrosis of the gastric mucosa. The hemorrhagic areas began in the blood vessels of the muscularis mucosae, destroying only the mucosa, and there was evidence of slow regeneration. The nonhemorrhagic type involved the mucosa and submucosa, but did not show signs of regeneration. He considered that the latter type might have resulted from arterial spasm due to the action of epinephrine, because he observed simultaneous intense congestion with signs of hemorrhage in the suprarenal gland on the side of resection. Section of the minor splanchnic nerve caused only occasional lesions, and of the major splanchnic nerve only transient congestion. Since both acute and chronic ulcers occurred, he did not consider that time was an important factor in their formation. Koennecke⁹⁶ observed that excision of the pylorus followed by a Billroth I or a Billroth II operation caused jejunal ulcer in one of five dogs, but bilateral division of the splanchnic nerves following the same procedure caused typical callous deeply penetrating ulcers in all dogs. He attributed this result to removal of an inhibition to secretion.

92. Schiff, J. M.: *Leçons sur la physiologie de la digestion*, Florence, H. Loescher, 1867, vol. 2, p. 557.

93. Quincke and Dättwyler, quoted by Bolton: *Ulcer of the Stomach*, London, Edward Arnold, 1913.

94. Durante, Luigi: *The Trophic Element in the Origin of Gastric Ulcer*, Surg. Gynec. Obst. **22**:399, 1916.

95. Dalla Vedova, Riccardo: *Ricerche sperimentali sulla patogenesi dell'ulcera gastrica*, Policlinico **6**:1153 (Suppl.) 1900.

96. Koennecke, W.: *Experimentelle Untersuchungen über die Bedeutung des Pylorusmagens für die Ulcusgenese*, Arch. f. klin. Chir. **120**:537, 1922; *ibid.*, Zentralbl. f. Chir. **50**:276, 1923; *Ulcusgenese und Gastroenterostomie*, *ibid.* **53**: 1866, 1926.

Celiac Plexus.—Gundelfinger,⁹⁷ after extirpation of the celiac ganglion (by which the action of the sympathetic was removed from the stomach and duodenum, leaving only vagal influence), succeeded in producing gastric lesions. Latzel⁷⁵ reported negative results after extirpation of the celiac plexus. Greggio, in his comprehensive review, reported ulceration of the gastric mucosa and hyperemia in the liver following extirpation of the celiac plexus by Pincus and Samuel, Löwin, Boer and Popielski; others have failed to produce them by this procedure in dogs and rabbits, for example, Adrian, Budge, Lustig, Lamansky and Peiper. Lesions of the plexus were found to produce ulcers and mucous hemorrhages by dalla Vedova,⁹⁵ Kawamura,⁹⁸ and Lilla and Gibelli.³⁵ On the other hand, Donati,⁹⁹ Kobayashi,⁴⁸ Lorenzi¹⁰⁰ and Schmincke¹⁰⁰ observed negative results or only small hemorrhages by irritation of the plexus. Brancati¹⁰⁰ found that ablation of the paravertebral lumbar sympathetic in a dog caused capillary dilatation, necrosis of the mucosa and ulcers at the pyloric region of the stomach and in the adjacent part of the duodenum.

The Vagi.—There has been a much more extensive investigation of the relationship of vagal influence to gastroduodenal lesions. Resection of both vagi in the neck of rabbits was found by Lorenzi to produce hemorrhage in the gastric mucosa fairly frequently. Saitta,⁴⁹ after bilateral vagotomy, observed multiple ulcers when he administered 3 per cent hydrochloric acid by mouth. Finzi¹⁰¹ noted that extirpation of one vagus yielded inconstant results, but that bilateral vagotomy produced, with greater regularity, circulatory disturbances, edema, ecchymosis, necrotic processes and atrophic ulceration. Keppich¹⁰² reported the formation of ulcer in five cases following resection of the vagus. According to Greggio, negative results following vagotomy in the neck of a rabbit are reported by Donati, Kobayashi, Körte and Martini; however, Midulla found that sectioning the vagus in the neck of frogs and

97. Gundelfinger, Ernst: Klinische und experimentelle Untersuchungen über den Einfluss des Nervensystems bei der Entstehung des runden Magengeschwürs, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **30**:189, 1918.

98. Kawamura, K.: Zur Frage der Verdauung lebenden Gewebes im Magen, zugleich ein Beitrag zur Pathogenese des runden Magengeschwürs, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **26**:379, 1913.

99. Donati, M.: Experimentelle Versuche das Magengeschwür vermittle Verletzungen der Magenerven hervorzurufen, Zentralbl. f. Chir. **31**:346, 1904.

100. Lorenzi; Schmincke, and Brancati, quoted by Greggio: Arch. de méd. expér. et d'anat. path. **27**:533, 1916-1917.

101. Finzi, Otello: Ueber Veränderungen der Magenschleimhaut bei Tieren nach Nebennierenextirpation und über experimentell erzeugte Magengeschwüre, Virchows Arch. f. path. Anat. **214**:413, 1913.

102. Keppich, Joseph: Künstliche Erzeugung von chronischen Magengeschwüren mittels Eingriffe am Magenvagus, Wien. klin. Wchnschr. **34**:118, 1921.

toads caused gastric dilatation, spasm of the pylorus, hypersecretion of the gastric juice, and ulcers which showed a tendency to become chronic and perforate.

The thoracic approach to the vagus has been utilized by others. Zironi,³³ after cutting the vagi around the esophagus of rabbits, observed ulceration in fifty-nine of 100 experiments. Antonini¹⁰³ observed ulcers in only seven of 100 animals after the same procedure; the day following operation there was gastric dilatation and congestion, with the development of lesions possessing the same gross and microscopic appearances as peptic ulcer in man. Cicatrization was not observed. In lesions observed after twenty, twenty-five and fifty days, there was no evidence of healing. Greggio frequently produced hemorrhagic infiltration of the mucosa after bilateral vagotomy, but in only one case did he find a chronic ulcer. This ulcer was 2 cm. in diameter and was situated on the greater curvature. He quoted negative results following this procedure by Krehl, Futsch, Kawamura, Rubaschoff, Muziolli and Fiori, and inconstant results by Samuelson and Contejan.

Thorough studies have been carried out following resection of the vagi in the abdomen. Zironi claimed to have produced gastric ulcer in sixty-four of 100 rabbits following subdiaphragmatic vagotomy. Lorenzi duplicated these observations. Van Yzeren cut both vagi subdiaphragmatically in twenty rabbits; in ten of them he found chronic single ulcers, usually near the pylorus; the earliest was observed in five days and the oldest in 289 days. Ophuls,¹⁰⁴ repeating these studies with the same results, concluded that the lesions were neurotrophic, and that trophic influences are necessary to preserve the normal resistance of the mucous membrane to the digestive action of the gastric juice. Latzel⁷⁵ noted hemorrhagic erosions and ulcerations in ten dogs following subdiaphragmatic vagotomy. Zironi, after similar resection in guinea-pigs, found lesions varying from 0.3 to 1 cm. in diameter in 63 per cent of his studies. Donati⁹⁹ reported negative results after a thorough study by this method. Greggio quoted Gunsburg and Lundi and Kobayashi and Marchetti as having caused diffuse changes in the mucosa or actual ulcers by this procedure; Saitta, Gibelli, Finachiaro, Lilla and Vigliani reported negative results.

Stimulation of the vagus has given contradictory results. Stahnke,¹⁰⁵ in studying the effect of long continued vagal stimulation on gastric

103. Antonini, Leopoldina: La resezione intratoracica laterale del vago nei suoi rapporti con la patogenesi dell' ulcera rotonda dello stomaco, *Riforma med.* 1:88, 1914.

104. Ophuls, W.: Gastric Ulcers in Rabbits Following Resection of the Pneumogastric Nerves Below the Diaphragm, *J. Exper. Med.* 8:181, 1906.

105. Stahnke, Ernst: Experimentelle Untersuchungen zur Frage der neurogenen Entstehung des Ulcus ventriculi zugleich ein Beitrag zur pathologischen Physiologie der Mageninnervation, *Arch. f. klin. Chir.* 132:1, 1924.

motility and secretion, faradized the vagi for forty minutes. At necropsy gastritis of the mucosa was found in some dogs, and superficial defects in the mucosa were found in others. He considered the ulceration to be a result of increased secretion and chronic gastritis. Keppich,¹⁰² by stimulating the vagi of rabbits with electrodes, produced chronic gastric ulcer in ten of eleven surviving animals. Westphal²⁵ believed that extreme vagal irritation explained the ulcers following the injection of pilocarpine. Hayashi interpreted similarly the lesions produced by muscarine. Gundelfinger was unable to produce ulcers by vagal irritation. Greggio cited Talma and Lichenbeld as having produced lesions by excitation of the vagus; Lorenzi and dalla Vedova, after burns and alcoholic injections into the vagus, caused hemorrhage and ulceration of the stomach. Negative results were reported by Korte and Donati.

The combination of these various procedures has given rather inconsistent results. Donati recorded negative results after abdominal section of the vagi and extirpation of the celiac plexus. According to Greggio, Samuelson noted negative results following the same procedure, with the administration of hydrochloric acid in addition; on the contrary, Lilla found that this surgical procedure alone yielded small punctate hemorrhages of the mucosa. Induced anemia seems to augment these neurotrophic lesions. Zironi increased the incidence of ulcer following thoracic and subdiaphragmatic resection of the vagi from 59 to 80 per cent by inducing artificial anemia; he also claimed to observe an acute ulcer assume chronicity coincident with induced anemia. Greggio caused lesions by vagotomy and the simultaneous administration of alcohol. Vagotomy associated with ligation of the pyloric artery and excision of the mucosa at a corresponding area produced complete healing and cicatrization in three months. Abdominal vagotomy with partial pyloric stenosis gave negative results. By injection of neurine which acts by paralyzing the motor, sensory and secretory terminal fibers to the stomach, Bedarida¹⁰⁶ produced trophic ulcers in the stomach of rabbits. Finally, Auer¹⁰⁷ induced ulcerous changes by removing all the nerve supply of the stomach, which resulted in paralysis, diminished movements and suppressed reflexes. Histologic studies of the terminal nerve endings in ulcers have been made by Perman, Nikolaysen and Askanazy, as reviewed by Okkels.¹⁰⁸ The latter found internal inflammatory

106. Bedarida, N. V.: *Produzione sperimentale di ulcera gastrica*, Arch. ital. de chir. 9:109, 1924.

107. Auer, quoted by Greggio: Arch. de méd. expér. et d'anat. path. 27:533, 1916-1917.

108. Okkels, H.: *Pathologic Changes in the Nerves of the Stomach Wall in Cases of Chronic Gastric Ulcer*, Am. J. Path. 3:75, 1927.

changes of the perineural sheath of nerve branches in the myogastric plexus, nerves embedded in connective tissue and proliferative central cicatrix neuromas. He considered these changes as secondary and non-specific, but believed that they may contribute to the chronicity of ulcers.

The theoretic interpretation of these results is of interest. Greggio concluded that vagotomy alters gastric motility, delays emptying of the chyme into the intestine, causing dilatation of the stomach and possibly interference with the mechanism of the pylorus. Von Bergmann¹⁰⁹ believed that hypertonicity of the vagus produces gastric spasm which puckers the gastric mucosa, strangles it and produces local ischemia and necrosis; this area is digested by the gastric juice and is eroded at its edges, and ulcer develops. Durante⁹⁴ conceived of central psychic stimuli changing the normal vasomotor tonus which might result in rupture of small arterial walls in the stomach, or toxic stimuli which might irritate the peripheral sympathetic system (the trophic nerve controlling the vasomotor nerves of the stomach) and lead to the formation of ulcer.

Glandular Influence.—The effect of glandular activity on the formation of ulcer may be viewed as associated with some type of nervous mechanism. Durante, it will be recalled, noted that ulcers following median splanchnic resections were associated with lesions of the suprarenal glands, and concluded that the effect might have been produced by suprarenal activity.

The studies of numerous investigators have indicated a possible relationship between the glands of internal secretion and the ulcerative lesions of the stomach. There are reported in the literature five cases of ulcer of the duodenum and stomach in man associated with thickening of the suprarenal capsule, hypertrophy, fatty degeneration, congestion and multiple hemorrhages into the glands. Latzel⁷⁵ reported the occurrence of ulcers in three animals following destruction of the suprarenal capsule. Greggio quoted Gibelli, Onde and Cioffi as having produced ulcer by induced suprarenal insufficiency. Mann¹¹⁰ observed acute ulcerations in 90 per cent of animals following the removal of both glands, but none associated with simple removal of the capsules. Hemorrhagic areas were found in the stomach in one animal which died in twenty-four hours; definite ulcers were found in another in twenty-two hours. If the ulcers were situated in the fundus (the pylorus being normal) usually the mucosa alone was involved; if they were in the prepyloric division they penetrated the muscularis mucosae. The duo-

109. Von Bergmann, G.: Das spasmogene Ulcus pepticum, München. med. Wchnschr. 60:169, 1913.

110. Mann, F. C.: A Study of the Gastric Ulcers Following Removal of the Adrenals, J. Exper. Med. 23:203, 1916.

denum was generally injected. The suggested dependence of these lesions on bile and trypsin was ruled out by their continued appearance after the establishment of a biliary and a pancreatic fistula. The acid appeared to be a factor as ulcers did not develop when sodium bicarbonate was fed to dogs on whom suprarenalectomy had been performed. Elliott¹¹¹ noted acute gastric ulcers following the removal of suprarenal glands in cats, and cited it as proof of the full digestive power of the gastric juice. Finzi¹⁰¹ observed edema, congestion, hemorrhage, necrosis and ulceration with an effort to heal following suprarenal suppression. Friedman¹¹² found lesions in the pyloric portion of the stomach to be most frequently associated with removal of the left suprarenal gland, and in the rest of the stomach associated with removal of the right suprarenal gland.

Friedman, while studying the interrelationship with other glands, also noted that removal of one suprarenal gland and one thyroid gland did not have any effect on the integrity of the gastric mucosa, but that intravenous thyroid medication associated with this procedure caused small ulcerations. Finzi also observed that the simultaneous removal of one thyroid gland and one suprarenal gland failed to cause ulcerous changes; he assumed that suprarenal insufficiency can manifest its action on the stomach only with an intact thyroid gland, and that the correlation of internal secretions may have a bearing on the formation of ulcer. Hardt⁵¹ studied the relationship of the feeding of thyroid gland to acidity and found that with increasing thyroid administration there was a decrease in acidity and gastric secretion, while with its interruption there was a return to the normal status. Hayashi, by imitating the so-called mixed stigmatized constitution with the administration of thyroid gland, was able to produce spasmogenic ulcerous changes. Greggio reported ulcers following thyroidectomy as having been produced by Boccardi, Grofredi, Falcone and d'Amore. He reported ulcers following exclusion of the liver by Mueller, Kollicher, Bidder and Schmidt, Beati and others. They have been observed by Bollman and Mann³⁸ following insufficiency of hepatic function induced by partial hepatectomy.

DIGESTIVE JUICES

Thus far, four principal fields of experimentation, vascular, bacterial, toxic and neurologic, have been reviewed. In evaluating the results obtained, one is justified in concluding that the occurrence of ulcer has

111. Elliott, T. R.: Some Results of Excision of the Adrenal Glands, *J. Physiol.* **49**:38, 1914-1915.

112. Friedman, G. A.: The Influence of Removal of the Adrenals and One-Sided Thyroidectomy upon the Gastric and Duodenal Mucosa: The Experimental Production of Lesions, Erosions and Acute Ulcer, *J. M. Research* **32**:287, 1915.

been variable. One investigator has observed results contradictory to those of another; true chronic indurated ulcers have been reported rarely. These studies, however, have answered a part of the problem; they have indicated a variety of means by which an initial acute lesion may be established. Probably only a few investigations (with the exception of Rosenow's work on the elective localization of bacteria) can be interpreted as of direct clinical significance. On the basis of these studies one is still confronted with the problem so aptly stated by Cohnheim in 1880: "The real difficulty in understanding simple ulcer of the stomach is not so much its mode of origin, as the circumstance that it usually so obstinately refuses to heal." He continued, referring to ulcers of embolic origin: "There must be in addition an unknown something which prevents the healing of ulcer. But whether, as has more than once been suggested, this something consists in an abnormal acidity of the gastric juice, we have as yet no positive investigation to show." Mann and his co-workers¹¹³ have probably supplied this desideratum. By "positive investigations" considerable evidence now indicates that the "unknown something" consists in the action of mechanical factors and the disturbance of the factors of acid and alkali at the pylorus. The mechanical factors and disturbance of the optimal chemical conditions for each side of the pylorus, which result from the surgical procedures employed in these studies, are probably the sole etiologic factors in causing the experimental ulcers, and possibly form the basis for the chronicity of clinical ulcers, determining their inability to heal.

Chemical Methods.—The importance of the digestive juices in relation to ulcer has long been suspected, and many investigations have been directed toward evaluating their influence. Saitta⁴⁹ administered 3 per cent hydrochloric acid by mouth following vagotomy and found multiple ulcers, whereas without the giving of acid he observed only hemorrhagic erosions. Friedman found that ulcers in the pyloric region, caused by the submucous injection of silver nitrate, became chronic when associated with hyperacidity produced by pyloric stenosis. Litthauer¹⁶ produced ulcer by administering 200 Gm. of hydrochloric acid to a dog, after ligation of gastric vessels and excision of a corresponding piece of mucosa. He also produced ulcers by feeding acid after having caused

113. Mann, F. C.: The Effect on the Jejunal Mucosa of Exposure to the Gastric Juice, *J. M. Research* **35**:289, 1917; A Case of Spontaneous, Acute and Subacute Peptic Ulcers and Carcinoma of the Thyroid in a Dog, *J. Lab & Clin. Med.* **6**:213, 1920-1921; Production and Healing of Peptic Ulcer: An Experimental Study, *Minnesota Med.* **8**:638, 1925; The Chemical and Mechanical Factors in Experimentally Produced Peptic Ulcer, *S. Clin. N. Amer.* **5**:753, 1925. Mann, F. C., and Kawamura, Kyoichi: An Experimental Study of the Effects of Duodectomy, *J. A. M. A.* **73**:878 (Sept. 20) 1919; Duodenectomy: An Experimental Study, *Ann. Surg.* **75**:208, 1923.

anemia by injection of pyrogallac acid. Gibelli¹¹⁴ failed to produce ulcers by simply administering acid by mouth. Bolton,¹¹⁴ as was noted under toxic manifestations, found that hydrochloric acid did not have any effect on the gastric mucosa under a concentration of 0.7 per cent, but that after a local lesion had been produced by the injection of gastrototoxin, concentrations as low as 0.25 per cent caused an increase in the size of the lesion. Acetic acid below a concentration of 2 per cent is innocuous, yet with the lesion once established by gastrototoxin a 0.5 per cent solution increased its size. Hydrochloric acid, the only digestive juice capable of attacking connective tissue, caused necrosis of granulation tissue in the base of the ulcer, and delayed healing of the ulcer. Bolton also delayed healing of ulcers in the rabbit by artificial hyperacidity, but he discounted the acid factor because he found that ulcers did not heal any slower with a high Pavlov pouch and acid stasis than with a low pouch and free drainage. Butsch¹¹⁵ claimed that acidity has some bearing on the formation of ulcer because of a higher occurrence in the Roux Y-anastomosis, in which the alkaline neutralizing factor is diminished. He also called attention to the fact that ulcer is rarely seen after anastomosis for carcinoma of the stomach, associated with diminished, or the absence of, acidity. Durante claimed that an excess of acid caused irritation and gastritis, epithelial desquamation, enlargement of the follicles and ultimately rupture and ulceration.

Smith¹¹⁶ studied the relationship of bile to ulceration of the gastric mucosa. He applied a mixture of bile and acid to the mucosa of the stomach, without effect. An interrupted application, however, first of bile alone, then immediately afterward of 0.5 per cent hydrochloric acid, caused a greenish-yellow pedicle and a precipitate from the mucus, with occasionally an underlying area of necrosed epithelium. The following day superficial necrosis of two-thirds the depth of the mucosa with leukocytic infiltration had occurred. Injection of bile and acid into the lumen of the stomach by a stomach tube or through the pylorus, during the period of digestion, caused excoriation, hemorrhagic infiltration and ulceration. He observed negative results in a stomach during fasting. After tying the esophagus and duodenum, he injected bile into the stomach for twenty-four hours; large quantities of bile alone caused hemorrhagic lesions; small amounts of bile with acid also caused lesions;

114. Bolton, Charles: The Part Played by the Acid of the Gastric Juice in the Pathological Processes of Gastric Ulcer, *J. Path. & Bact.* **20**:133, 1916.

115. Butsch, J. L.: Ulcers of the Gastro-Intestinal Tract with Special Reference to Gastro-Jejunal Ulcers. Papers from The Mayo Foundation and the Medical School of the University of Minnesota, Philadelphia, W. B. Saunders Company, 1915-1920, vol. 1, p. 57.

116. Smith, G. M.: An Experimental Study of the Relation of Bile to Ulceration of the Mucous Membrane of the Stomach, *J. M. Research* **30**:147, 1914.

bile injected with a 5 per cent solution of sodium bicarbonate did not produce lesions except in one instance. He concluded that the presence of acid is necessary for the injury of the mucosa by bile. He quoted Rywosch as having produced inflammation and gangrene of the stomach of rabbits by feeding an excess of bile salt. Oddi and Dastre¹¹⁷ did not get these results following cholecystogastrostomy. Smith concluded that it must be conjectured whether in man the bile may become a source of injury to the epithelium, particularly since it normally regurgitates through the pylorus into the stomach. Sellards¹¹⁸ studied the effects of bile salts by injecting sodium glycocholate intraperitoneally. He produced large hemorrhagic areas in the stomach and ulceration of the mucosa. The subcutaneous injection of bile or bile salts produced similar lesions. Small repeated doses tended to localize ulcers near the pylorus. Since there were only a few minute lesions in the lungs and intestines, Sellards claimed for the bile salts a specific action on the gastric mucosa.

Such methods of studying the influence of the digestive juices are limited both in variety of experimental procedures and in the lack of control of physiologic reactions. Recourse must be had to surgical methods in order to determine the nature of the physiologic interrelationship of the juices. It is true that unphysiologic conditions may be established by such surgical measures, but as hepatectomy makes it possible to study the function of the liver and pancreatectomy to study the function of the pancreas, so the surgical procedures which have resulted in the formation of ulcer disturb the normal status (as nature may do with greater finesse), and produce effects which make it possible to analyze the significance of the juices from the point of view of formation of the ulcer.

Surgical Methods.—Kapsinow¹¹⁹ excluded the bile from the digestive tract by implanting the fundus of the gallbladder into the pelvis of the right kidney (cholecystonephrostomy). When healing was complete he ligated and divided the common duct. The animals lost weight and refused food, and tarry stools developed. Necropsy was performed in two or more weeks. In seventeen of forty-three animals single or multiple ulcers from 2.5 to 5 cm. in diameter, with punched-out overhanging edges were formed. They extended to or perforated the serosa. Kapsinow quoted Whipple as having produced ulcer after ligating the

117. Oddi, R., and Dastre, A., quoted by Smith: J. M. Research **30**:147, 1914.

118. Sellards, A. W.: Ulceration of the Stomach and Necrosis of Salivary Glands Resulting from Experimental Injection of Bile Salts, Arch. Int. Med. **4**: 502 (Nov.) 1909.

119. Kapsinow, R.: The Experimental Production of Duodenal Ulcer by Exclusion of Bile from the Intestine, Ann. Surg. **83**:614, 1926.

common duct in the presence of a biliary fistula, but he criticized the work because of the possibility of infection ascending through the fistulous tract. Gundermann,³⁷ after simple ligation of the common duct, observed the same symptoms of hepatic dysfunction as after partial ligation of the portal vein, namely, cerebral, renal and gastroduodenal disturbances, the stomach and duodenum showing hemorrhages and ulcerations. Smith anastomosed the gallbladder to the stomach with and without ligation of the common duct, but results were negative in both instances. He reported negative results after the same procedure by Oddi and Dastre. Beaver,¹²⁰ likewise, did not observe ulcers following cholecystogastrostomy and ligation of the common duct. As stated, Greggio quoted Mueller, Köllicher, Bidder and Schmidt, Beati and others as having noted ulcers after exclusion of the liver. Bollman and Mann³⁸ reported that ulcers had perforated following partial hepatectomy, true Eck fistula and ligation of the common duct, procedures which probably influenced the quantity of bile entering the duodenum.

Little study has been made of the effect of excluding the pancreatic juice alone. Jona,⁷⁶ after tying the pancreatic duct in eleven animals, found ulcers of the duodenum, stomach and jejunum which he ascribed to lack of neutralization of the acid chyme. Gallagher²⁹ observed delayed healing of traumatic ulcers of the duodenum after ligation of the pancreatic duct.

The combined elimination of the bile and pancreatic juice has been studied thoroughly. Kehrer¹²¹ implanted the pancreatic duct into the appendix or lower part of the ileum and anastomosed the gallbladder to the same site, ligating the common duct. In six animals that died at different intervals, he found marked injury to the wall of the stomach. Necropsy after thirteen, twenty-five and sixty-four days disclosed superficial circumscribed necrosis with deeper necrosis in three other dogs on which necropsy had been carried out after nine, twenty-five and 100 days. Macroscopically and microscopically, they were typical ulcers. Mann and Williamson¹²² studied the production of ulcer in the duodenum, following transplantation of both the bile and the pancreatic ducts into the lower part of the ileum. The ulcers produced were single and multiple, indurated, varying from 1 to 3 cm., and were situated in the region between the pylorus and the ampulla of Vater.

Mann was the first to study the formation of ulcer following the entire elimination of all the duodenal alkaline juices. The historic development of his ideas show clearly the underlying factors in these studies.

120. Beaver, M. G.: Personal communication to the author.

121. Kehrer, J. K. W.: Ueber die Ursache des runden Magengeschwüres, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **27**:679, 1914.

122. Mann, F. C., and Williamson, C. S.: The Experimental Production of Peptic Ulcer, *Ann. Surg.* **77**:409, 1922.

While investigating the problem of whether or not the duodenum produced a secretion essential to life, he devised a one-stage operation, excising the duodenum, anastomosing the jejunum to the transected pylorus and then implanting the pancreatic and bile ducts into the anastomosed jejunum. In two of ten dogs operated on, peptic ulcer resulted. Mann and Williamson then transplanted the bile and pancreatic ducts into the ileum, from 30 to 50 cm. from the cecum. Definite ulcers developed in ten of thirty-one animals (five ulcers were chronic). Removal of the duodenum and anastomosis of the jejunum to the pylorus, with transplantation of the bile and pancreatic ducts into the distal part of the ileum, resulted in ulcers in eight of the ten dogs operated on. The procedure was then simplified by devising the "duodenal drainage" operation. By this method the duodenum was isolated by transection at the pylorus and at the upper part of the jejunum. The pyloric end of the duodenum was closed in and the distal end anastomosed to the distal part of the ileum; the free end of the jejunum was anastomosed to the pylorus. With the duodenal alkaline juices drained into the ileum, the acid chyme of the stomach drained into an unprotected jejunum. Definite ulcers developed in fourteen of sixteen animals. They were usually situated a few millimeters from the gastrojejunal anastomosis. They developed usually within one or two months after operation, were from 4 to 15 mm. in diameter and penetrated to various depths. A gray covering first appeared over an area on the mucosa where killed, coagulated cells were present. Hemorrhage occurred between the adjacent tubules. As the mucosa disappeared, leukocytic infiltration developed, and the process penetrated the muscularis mucosae. Perforation occurred in from forty-eight to sixty hours, chronicity was established in three weeks, or the lesion was the same at the end of five months as at the end of one month.

In evaluating the factors involved in this result, Mann conceived of the acid chyme as being ejected through the pylorus by the gastric contractions, as if through a nozzle, and impinging forcibly against the wall of a segment of intestine containing little, if any, alkali; the mechanical and chemical action of this stream led to necrosis of the epithelium and the formation of ulcer.

The degree of acidity and the amount of acid to which the ulcer-bearing area is subjected depends normally on the balance at the pylorus between the gastric acid chyme and the alkaline secretions of the duodenum. The combined intestinal, pancreatic and biliary secretions must be sufficient to neutralize the acid chyme passing the pylorus to from 0.12 to 0.14 per cent, as shown by Boldyreff.¹²³ Mann showed that if,

123. Boldyreff, W.: The Self-Regulation of the Acidity of the Gastric Contents and the Real Acidity of the Gastric Juice, *Quart. J. Exper. Physiol.* 8:1, 1915.

after a duodenal drainage operation, the duodenal juices were drained back into the jejunum just distal to the gastrojejunal anastomosis, so that such neutralization did occur in the ulcer-bearing region, a lesion did not develop. Morton similarly showed that secondary anastomosis of the closed duodenum to the jejunum after surgical duodenal drainage, so that alkalis drained back at the site of ulcer, led to the healing of an existing ulcer.

By several experimental methods, Morton¹²⁴ further confirmed the idea that the chemical and traumatic factors are of major importance in establishing chronicity in ulcers and failure to heal. He excised pieces of mucosa from the lesser curvature in dogs after the duodenal drainage operation, and showed persistence of the defect in from 50 to 62 per cent of those in the antrum after a period of two weeks. This was in contrast with normal controls, in which similar areas with excised mucosa healed in two weeks, with complete epithelization. Incidentally, after excision of mucosa from the greater curvature of the antrum in drainage operations healing was more rapid, showing that whatever the factors that prevented healing, they were more active on the lesser curvature. Finally, Morton transplanted jejunal patches with an intact circulation into several different areas in the gastric wall of dogs on which duodenal drainage had been performed. In thirteen cases, four ulcers developed on the patches. Again suggesting the greater activity of the destructive forces on the lesser curvature, three of these ulcers developed in patches on the lesser curvature, and only one on a patch elsewhere. This is in contrast with Morton's control studies (and corroborating earlier work by de Takats and Mann¹²⁵), in which only one ulcer developed in jejunal patches on the lesser curvature and none on patches in other parts of the stomach in a series of normal dogs. The observations extended over a period of from thirty-six to 419 days.

Mann considered the active mechanical factor in the duodenum to be the force of the impinging stream ejected through the pylorus. In the stomach, Morton considered the mechanical factors chiefly active in localizing the ulcers as the paucity of protecting rugae in the prepyloric segment, particularly along the "Magenstrasse" with its poor blood supply, and the convergence of the lines of force along the lesser curvature, as suggested by Aschoff.¹²⁶

124. Morton, C. B.: Observations on Peptic Ulcer: IV. Patch Transplants of Jejunum in Stomach, *Ann. Surg.* **85**:879, 1927.

125. De Takats, Geza, and Mann, F. C.: The Effect on the Jejunal Mucosa of Transplantation to the Lesser Curvature of the Stomach, *Ann. Surg.* **85**:698, 1927.

126. Aschoff, Ludwig: Lectures on Pathology, New York, Paul B. Hoeber Company, 1924, p. 358.

I. EFFECTS PRODUCED BY DRAINAGE OF THE DUODENAL SECRETIONS BACK INTO THE STOMACH: MECHANICAL FACTORS

The following report represents my work on peptic ulcer produced experimentally by the methods devised by Mann. The principle of the methods used by Mann and his co-workers consists essentially in shunting the alkaline secretions of the duodenum away from the pylorus so that the gastric juice and chyme are not neutralized. This has been accomplished by operations such as transplantation of the bile and pancreatic ducts into the distal part of the ileum, or by Mann's method of surgical duodenal drainage.

As stated in the preceding review, Mann and Williamson demonstrated the occurrence of ulcer in the duodenum in about 50 per cent of the dogs in which the bile and pancreatic ducts had been transplanted into the distal part of the ileum. Morton showed that, following surgical duodenal drainage, peptic ulcers formed in the anastomosed jejunum in approximately 100 per cent of experiments. He also found that, whereas in the normal dog traumatic lesions of the gastric mucosa healed readily, following a duodenal drainage operation such lesions tended to become chronic peptic ulcers. In a similar way he demonstrated a greater tendency toward ulceration of transplants of jejunal patches in the gastric wall in dogs subjected to duodenal drainage than was the case in normal dogs.

METHODS

In the present study the operation of surgical duodenal drainage was modified in such a way that while eliminating the alkaline secretions from the distal side of the pylorus they were shunted to the gastric side. This was accomplished by draining the duodenal secretions into the fundic portion of the stomach rather than into the distal part of the ileum. It was an apparent assumption that these alkalis might control the acid factors in the stomach and thus prevent the formation of the ulcers which developed after total elimination of the alkalis.

• The same type of dogs used in the former studies were used in these experiments. All surgical procedures were carried out with the dogs under ether narcosis. Careful aseptic technic was observed throughout. Clamps were not used at the lines of anastomosis. Absorbable catgut was used for all intestinal suture work.

The abdomen was opened by a high median line incision. The pylorus was exposed and the vessels and nerves to the upper border were cut between two ligatures. The pylorus was severed, and the duodenal end was inverted. In like manner, the jejunum was severed just distal to the ligament of Treitz. The distal end was brought up and anastomosed to the open gastric end of the pylorus, thus reestablishing the continuity of the tract, with the duodenum excluded. The distal end of this isolated duodenum was anastomosed to the fundic portion of the stomach. This was done by *end-to-side anastomosis*, or by *side-to-side anastomosis* following closure of the distal end. These anastomoses were made on either the anterior or the posterior surface of the stomach. The type of anastomosis employed did not have any influence on the end-results of the experiment (fig. 1).

The modified technic of surgical duodenal drainage established a new type of disturbance of the relationship between the gastric chyme and the duodenal juices. The whole volume of duodenal alkalis, during their entire secretory cycle, was shifted from the distal side of the pylorus into the fundic portion of the stomach. These duodenal secretions were now retained in the upper part of the digestive tract, were freely intermixed with the gastric juice, and in this state passed through the pylorus into the jejunum (now unprotected by alkalis) and on into the intestinal tract (fig. 2). The significant question was: Could these alkalis which emptied into the stomach control the acidity of the gastric juice and thus prevent the formation of ulcers?

After operation, food was withheld for from two to three days. The dogs recovered quickly from the effects of the operation and were placed on routine kennel care. They were fed regularly with kennel food, and supplementary feedings of milk and syrup were given if they lost weight.

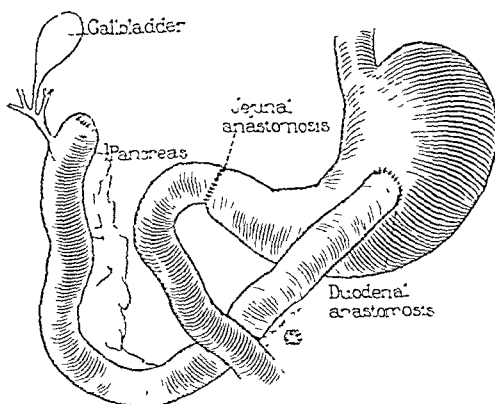


Fig. 1.—Operative procedure, showing the duodenum draining the secretions of the gallbladder, liver and pancreas into the fundic portion of the stomach.

RESULTS

Types of Ulcer.—Following the operation typical ulcers of the jejunum, such as were reported in all the earlier studies by Mann and his colleagues, formed in approximately 80 per cent of a series of twenty-six dogs. This figure is slightly lower than in the other series, which can be accounted for by the fact that two dogs were etherized because an ulcer was suspected; at necropsy, an ulcer was not found. Two other dogs in this series are still living two years after the operation, and the presumption is that ulcers have not developed. These four dogs have lowered the percentage of occurrence of ulcer.

The ulcers usually formed within from one to three months. Some of them perforated, causing sudden death. Others were first suspected when the dogs began to refuse food and lose weight. If the dogs were etherized at this time, ulcers of the anastomosed jejunum were usually found. The variations in the length of time in which the ulcers formed

preclude the possibility that operative trauma, thrombosis of vessels or cachexia are the essential factors concerned in producing these lesions.

Usually single, but sometimes multiple, ulcers were found. They were situated just beyond the suture line, and were usually regressive up to the gastric mucosa. If they were multiple they were distributed over an area of from 5 to 7.5 cm. of the upper part of the jejunum. The acute ulcers were cleanly punched out, suggesting a rapidly progressing type of lesion. The three layers of the intestinal wall, the

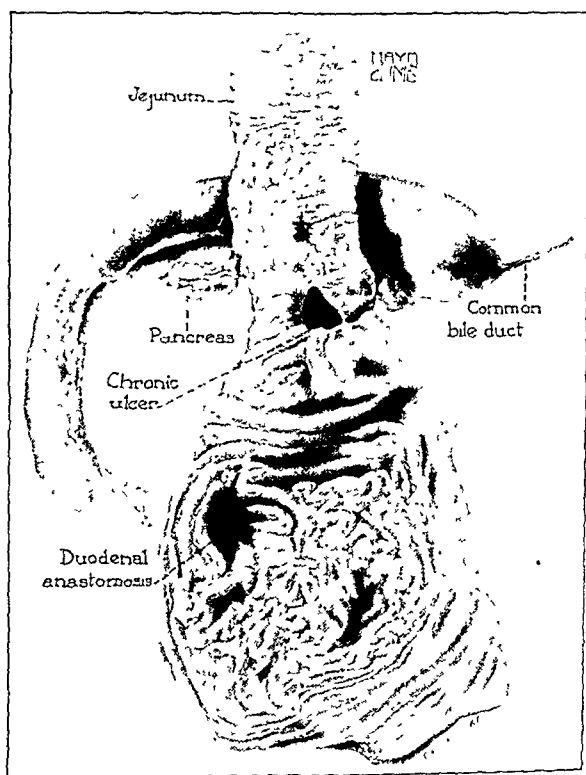


Fig. 2.—Anastomosis of the distal end of the duodenum to the fundic portion of stomach, thus draining the alkalis into this segment. The gastric chyme with the duodenal alkalis intermixed empty into the unprotected jejunum. A chronic ulcer appears at the usual site of formation.

mucosa, muscularis and serosa, were all extensively involved. Even these ulcers were not truly acute, in that the edges of the lesion were slightly indurated, suggesting some of the tissue reaction responsible for chronicity in other specimens (fig. 3).

The subacute ulcer, which was the type most frequently seen, gave definite evidence of early chronicity. The edges of the crater were thickened, due to the round cell infiltration from the tissue reaction.

There was graded involvement of the three coats in a terraced manner. The mucosa was ulcerated most extensively, its edges indurated, rounded and overhanging. The muscularis was eroded less widely, and the serosa least of all. The occurrence of ulcers, without contact at the suture line,

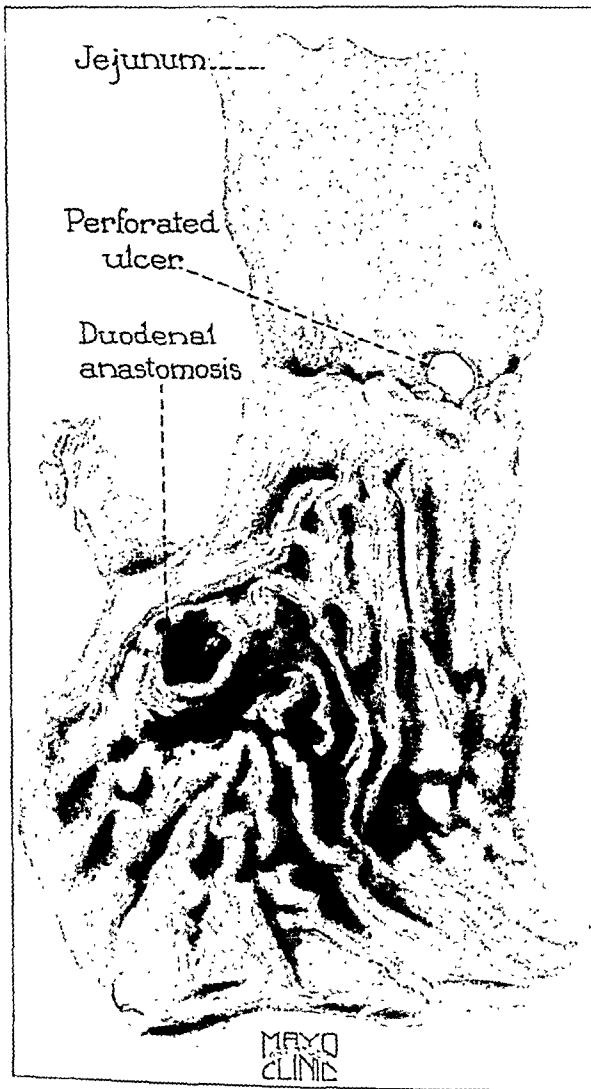


Fig. 3.—Acute ulcer of the jejunum following surgical duodenal drainage. Encroachment on line of anastomosis, with gastric mucosa intact.

indicates that the ones which encroach on the suture line are regressive (fig. 4).

The chronic indurated ulcers possessed all the characteristics of the crater type of ulcer observed in man. They were of considerable depth,

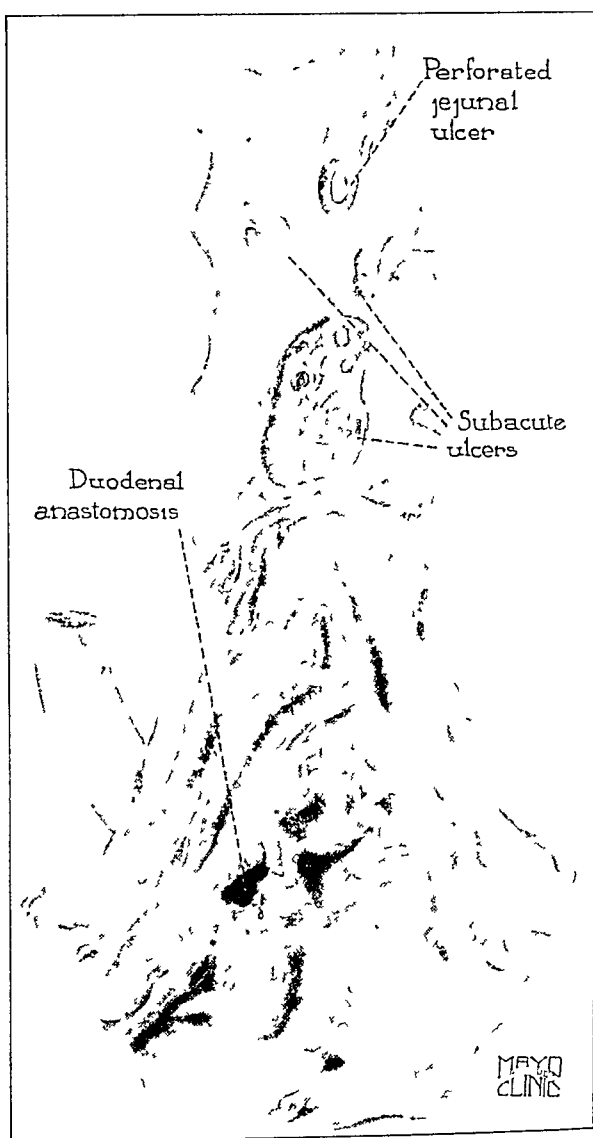


Fig 4—Subacute types of ulcer with less extensive ulceration of underlying muscularis and serosa than of the mucosa. Ulcers at considerable distance from line of anastomosis

from 6 to 10 mm., with sloping indurated walls. The mucosa was thickened and overhung the sloping walls. The base of these chronic ulcers was usually formed by the peritoneal surface of an adjacent organ, such as the liver, onto which they had slowly perforated. This slow perforation afforded the tissues an opportunity to establish a more intense reaction which is characteristic of chronicity, that is, round cell infiltration and fibrosis (fig. 5).

Mechanical Factors.—The basis for the production of these experimental ulcers has been attributed mainly to the mechanical and chemical factors involved in the physiologic functions of this region. Two of the specimens in this series presented significant evidence of the influence of

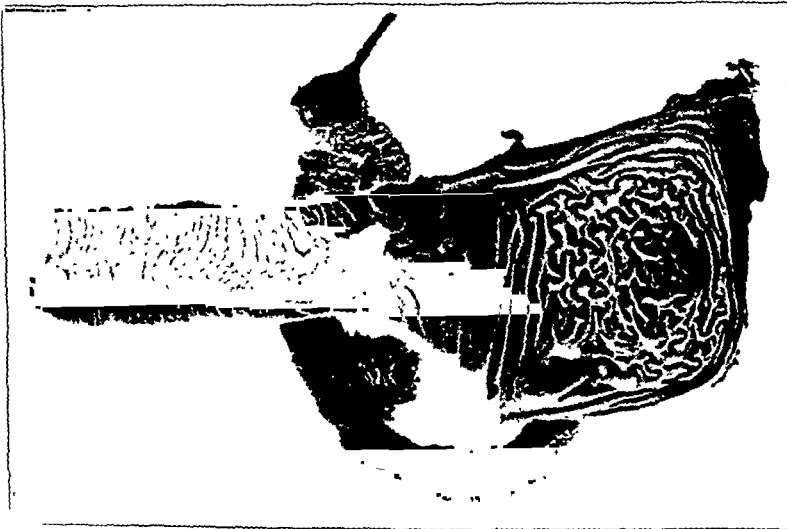


Fig. 5.—Typical chronic indurated crater type of ulcer. Small perforation in base of ulcer was penetrating onto lobe of liver, which saved the animal from death by perforation.

the two mechanical factors involved: the force of the stream ejected through the pylorus and the friction of coarse cellulose foods.

In the first specimen, a chronic peptic ulcer about 6 mm. in depth was present; fifty or more hairs from the dog's hide were embedded in the sloping wall of the distal half of the crater. There were only one or two hairs in the proximal half of the ulcer. Apparently, the chyme was ejected through the pylorus and impinged on this segment of the intestine with force sufficient to embed the hairs in the wall of the ulcer. This, of course, is not controlled proof, but it is suggestive evidence of the mechanical factor established by the passage of chyme from the stomach (fig. 6).

The other mechanical factor, the destructive friction of coarse cellulose foods on the delicate granulations and epithelial cells of a heal-

ing ulcer, was strikingly illustrated by the second specimen. The dog died suddenly from a perforated ulcer. At necropsy the peritoneal cavity did not show gross peritonitis. In the jejunum, just distal to the suture line, was a perforated ulcer through which protruded about 0.3 cm. of the tip of a moderate-sized pyramidal piece of turnip, a constituent of the mash fed to the dogs. The jejunum was carefully opened so as to leave the piece of turnip undisturbed. The lumen of the bowel and stomach contained a considerable quantity of bloody fluid, all of which was retained within the lumen of the viscera, because the ulcer had

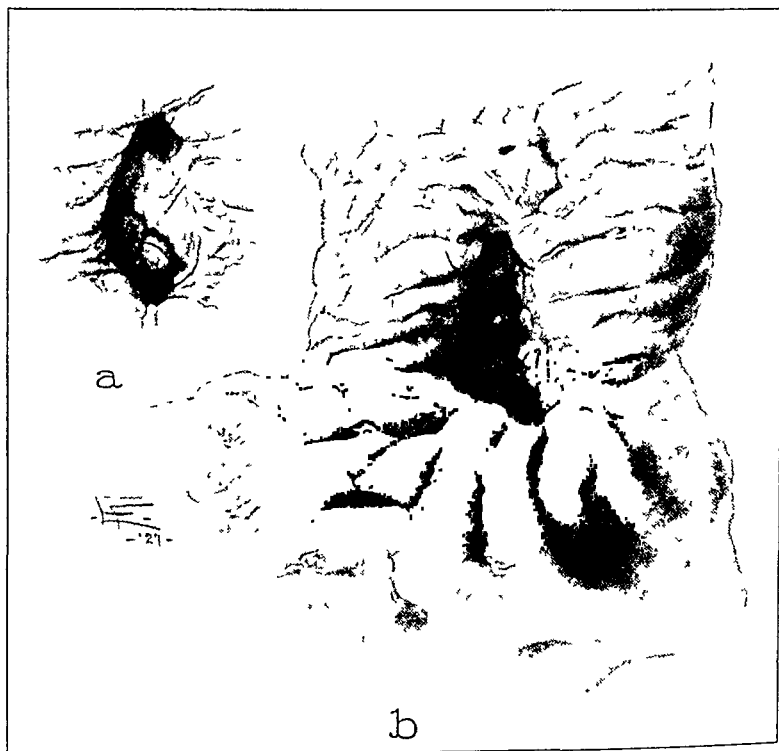


Fig. 6—*a*, absence of hairs in proximal end of ulcers; *b*, hairs embedded in the distal half of the crater of the ulcer

been completely occluded by the turnip which had perforated it. This perforation of an ulcer represents a most extreme degree of destruction by the friction of food (figs. 7 and 8).

COMMENT

In the early studies by Mann and his colleagues in which the original method of surgical duodenal drainage had been used, ulcers were produced by entirely eliminating the alkalis from the pyloric region and exposing the segment beyond the pylorus to the full autolytic action of

the gastric chyme. In the present studies the alkalis are still retained in the upper part of the intestinal tract but proximal to the pylorus; this allowed the uncontrolled autolytic action of the gastric chyme to persist beyond the pylorus. The resulting lesions indicated that one rôle of the alkalis, in the normal physiologic relationship, is to prevent the

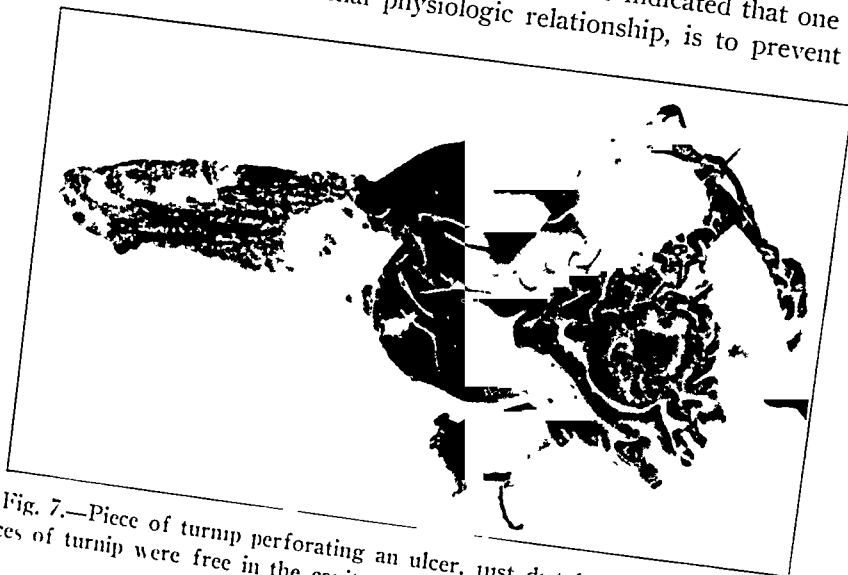


Fig. 7.—Piece of turnip perforating an ulcer, just distal to the pylorus; other pieces of turnip were free in the cavity of the stomach.

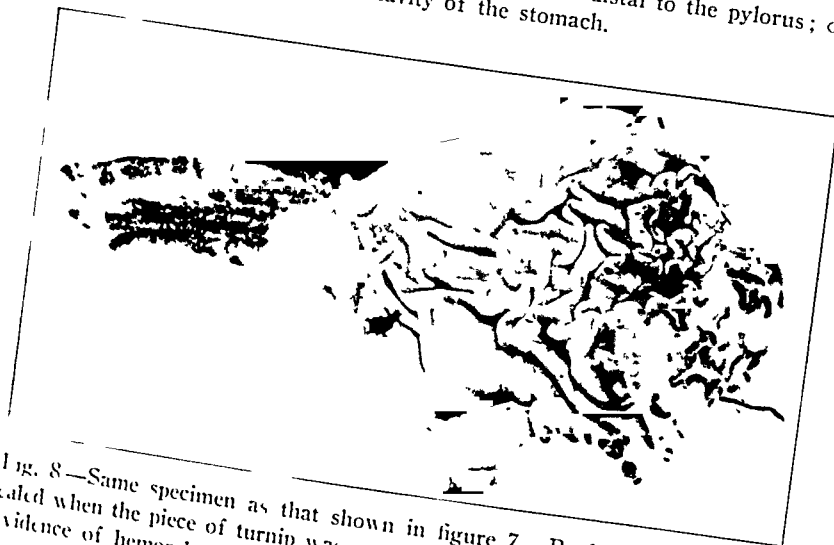


Fig. 8.—Same specimen as that shown in figure 7. Perforated type of ulcer revealed when the piece of turnip was removed. Discoloration of the bowel points to evidence of hemorrhage.

formation of ulcer, not by any specific protective action, but by some type of buffer or diluting action beyond the pylorus that terminates the acid peptic activity of the gastric chyme.

The results of these experiments emphasize the importance of the mechanical factors in causing chronic peptic ulcers. The specimen in

which the hairs from the dog's hide were found embedded in the distal half of the ulcer constitutes an observation just as suggestive as if particles of carbon had been mixed with the dog's food and these had been observed in the wall of the ulcer. The specimen indicates the force with which the stream ejected through the pylorus impinges on the site of ulcer formation.

The destructive action of coarse cellulose food is apparent when the delicate mechanism involved in the healing of an ulcer is considered. Morton, summarizing the experimental work done on the healing of ulcer, stated that Mann observed:

The base of the lesion is first cleaned, the slough separates, and a protecting coat of serum and coagulum forms over healthy granulations. These processes ordinarily take about four days. Simultaneously the mucosa begins to grow out from the edges as a thin layer of flat epithelial cells. The edges of the mucosa tend to overhang and the granulations to push up in the center, so that the growing edge of mucosa is protected in the resulting depression. This initial stage which has the effect of also decreasing the area to be healed over takes place in about ten days. Once initiated, the healing, if undisturbed, is rapid. In twenty days three-fourths or more of the base is covered with epithelium, and in thirty days the lesion is usually healed entirely. The scarring is in many cases hardly noticeable.

How easily this delicate mechanism might be compromised by the influence of friction was suggested by the piece of turnip which had perforated an ulcer. If a large piece of cellulose food could exert so destructive an influence, it is reasonable to assume that cellulose food of varying degrees of coarseness would exert a graded amount of friction, thus continually aborting the reparative tendencies of an ulcer.

That the assumption is justified is borne out by the experience of Bollman and Mann with dogs on whom an Eck fistula had been made. In a considerable percentage of the dog's acute perforated ulcers of the duodenum developed while they were fed on coarse food which contained much cellulose material. When the coarse foods were replaced by a soft or liquid diet, the occurrence of ulcers was decreased. This observation affords control evidence that with a partial deficiency (qualitative or quantitative) of the bile in the duodenum, the presence or absence of coarse cellulose food was the important factor in determining the frequency of the formation of ulcers in the duodenum.

On the gastric side of the pylorus there are two factors which would augment the friction of coarse cellulose food in the prepyloric segment, and thus greatly influence the localization of ulcers in this segment, as occurs clinically, and as reported in Morton's experiments. The first factor, as Morton pointed out, is the anatomic arrangement of the mucosa in this segment, which is closely attached and does not form protective rugae such as are found in the fundic portion of the stomach. This is particularly true of the lesser curvature. It is interesting to note

that there is total absence of such rugae in the duodenum and jejunum, which are most subject to ulceration and would thus permit maximal friction by coarse cellulose food.

The second and probably a highly important factor in augmenting the friction of cellulose food in the stomach is the type of motor activity in the prepyloric segment which I observed while working with the test meal of meat. In response to this adequate stimulus, the whole prepyloric segment was thrown into vigorous tonic contraction, so that it appeared sausage-shaped. Frequent peristaltic waves traversed the segment during early digestion, being superimposed on this tonic contraction. In contrast to this activity, the fundus appeared like a big motionless ball, with a simple wavering around its periphery. Pieces of cellulose food caught between the approximated, vigorously contracting walls of the prepyloric segment might exert considerable destructive friction on the reparative granulations and epithelial cells of an ulcer. If these particles were rejected at the pylorus and driven back into the fundus, as indicated by Cannon's study, the friction of each particle might be multiplied many times.

SUMMARY OF STUDY I

In this study, the technic of surgical duodenal drainage was so modified that the alkaline secretions of the duodenum were shunted from the distal side of the pylorus into the fundic portion of the stomach. Despite the volume of alkalis drained into the stomach, ulcers still formed in the anastomosed jejunum in approximately 80 per cent of the experiments.

Evidence was obtained which substantiated Mann's interpretation of the important mechanical factors that are active in causing these experimental ulcers, and which probably influence the localization of clinical ulcers. On the duodenal side of the pylorus these are the result of the force of the impinging stream ejected through the pylorus, and of the destructive friction of coarse cellulose foods on the reparative granulations and epithelial cells of a healing ulcer. On the gastric side of the pylorus there is the same friction of coarse cellulose food augmented in the prepyloric segment by the absence of protective rugae, particularly on the lesser curvature, and by the vigorous tonic and peristaltic contractions of this segment which appear in response to an adequate meal.

II. THE CHEMICAL FACTORS IN EXPERIMENTALLY PRODUCED PEPTIC ULCER

The present study was an investigation of the chemical factors involved in the development of the peptic ulcers produced by the experimental procedures devised by Mann. Former experiments have indicated fairly definitely the mechanical factors which influence the

development and localization of the ulcers. The active chemical factors have been suggested by the nature of the disturbed physiologic function. The rationale of the methods is best indicated by Mann's own words:

Our results in a preliminary series of experiments in which acid was administered orally, as well as the results of previous investigators, demonstrated that simulating the so-called "hyperacidity" and "hypersecretion" by the artificial administration of acid would be very difficult. The upper part of the intestinal tract can be subjected to an acid medium just as effectually by injuring the alkali-producing mechanism as by the administration of acid. We, therefore, undertook to eliminate singly and in combination, the various constituents of this mechanism, and it was found that injury of any one of these constituents caused the development of typical chronic peptic ulcer in a small percentage of experiments. We finally devised a method which consisted essentially in draining the alkaline secretion which is poured into the duodenum, into the ileum at a considerable distance from the point of emergence of the acid from the stomach into the intestine. Following this procedure, a typical peptic ulcer developed in a high percentage of experiments.

These ulcers, he thought, resulted from a disturbance of the normal relationship between the gastric and duodenal juices beyond the pylorus, besides the mechanical factors of that region.

The nature of this disturbed relationship between the gastric and the duodenal juices has never been exactly determined. Mann showed that an acid reaction to litmus persisted far down the intestinal tract following surgical duodenal drainage, whereas normally the reaction is alkaline to litmus. This was the basis of his idea that the acid chyme which passed the pylorus was not neutralized and acted as a major factor in the development of these ulcers.

Two hypotheses suggest themselves as to the nature of the disturbed relationship of the secretions resulting from this procedure. First, if Boldyreff's theory is accepted that the acidity of the gastric juice is regulated by regurgitation of duodenal alkalis into the stomach, then these procedures would injure this mechanism so that the mucosa would be exposed constantly to highly concentrated acid. This persistent state of hyperacidity might account for the production of the ulcers. If this theory is not true and the acidity of the gastric contents is independent of regurgitation of the duodenal alkalis, then the second hypothesis is probable, namely, that the acid peptic activity of normal gastric chyme causes these ulcers, because its action is not terminated beyond the pylorus following the loss of diluting or buffer secretions, bile and pancreatic juice. It is important to know which hypothesis is true, because, if it is the second one, these experiments have demonstrated the highly destructive action of the normal gastric chyme under experimental conditions which allow it to ulcerate the mucosa.

METHOD

By a method of fractional gastric analysis that I devised¹²⁷ for use on the normal dog it is possible to measure the effect of these procedures on the chemical changes of the gastric contents during digestive activity and during rest. This method, which I shall report in more detail elsewhere, consists in feeding a fasted animal with a meal of meat and water. Half an hour after feeding, single specimens are aspirated every thirty minutes until free acid appears. Then the aspirations are made every fifteen minutes until the free acid is neutralized. Chemical determinations are made for total and free acids, and these are charted. The total chlorides are titrated, and the chlorine value of the free acid deducted, so that the resulting figure, which is charted, indicates the chlorine value in neutral or combined form.

Three groups of dogs were operated on so as to repeat the methods used in the whole series of studies by Mann and his colleagues. Studies with the fractional

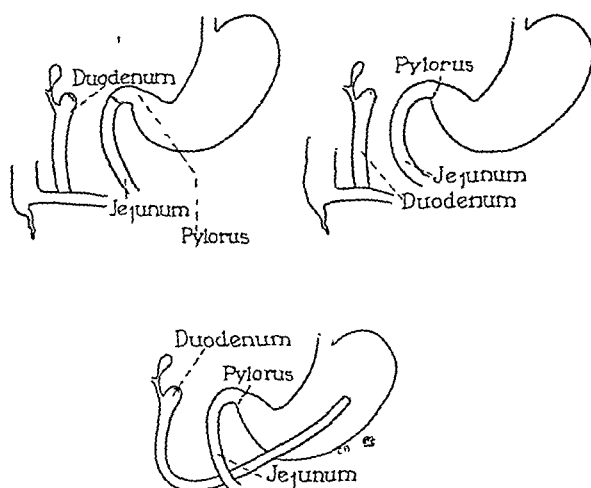


Fig. 9.—Three types of operative procedures: modified surgical duodenal drainage with section in first portion of duodenum; surgical duodenal drainage with section at pylorus; surgical drainage of duodenal alkalis into fundic portion of the stomach.

test meal of meat were made before and after the operations. The three procedures were as follows (fig. 9):

1. *Modified Surgical Duodenal Drainage.*—The usual type of drainage operation was modified by sectioning the first portion of the duodenum at the middle, rather than sectioning the pylorus. The duodenojejunal flexure was sectioned beyond the ligament of Treitz. The proximal end of the duodenum was closed in, and the distal end was anastomosed to the distal part of the ileum. Duodenojejunal anastomosis was made beyond the pylorus after the lumen of each segment had been enlarged by a longitudinal incision, thus obviating any mechanical dysfunction from stenosis at the line of anastomosis. Furthermore, nerves or significant blood vessels were not severed in the procedure.

127. McCann, J. C.: Unpublished data.

2. *Surgical Duodenal Drainage*.—The original method was used for this group. The nerves and vessels to the upper border of the duodenum were cut between ligatures. The pylorus itself was severed and the usual anastomoses made: the jejunum to the pylorus, and the closed duodenum to the distal part of the ileum. Thus all the disturbances of motor function present in the early studies as a result of the manipulations at the pylorus were present in this group.

3. *Surgical Duodenal Drainage Back into the Stomach*.—The technic was the same as that reported in the preceding study. The pylorus was severed and the duodenal end inverted. The duodenojejunal flexure was severed just distal to the ligament of Treitz. The distal end of the jejunum was anastomosed to the open gastric end of the pylorus. The distal end of the isolated duodenum was anastomosed to the fundic portion of the stomach. Thus the whole volume of duodenal alkalis was shifted from the distal side of the pylorus into the fundic portion of the stomach.

RESULTS

In the first procedure, since the duodenum rather than the pylorus was severed, all impediments to normal emptying were avoided. As

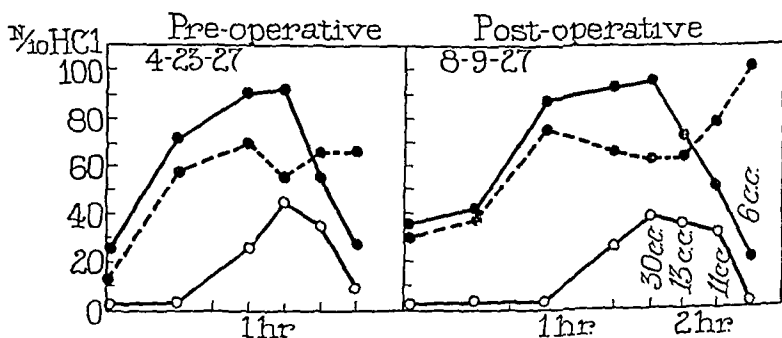


Fig. 10.—Chronic ulcer; the same essential character of curves occurred in response to a test meal before and after the surgical drainage of the duodenal alkalis from the pylorus into the distal part of the ileum; anastomosis in the middle of the first portion of the duodenum. In this and the following charts, the solid line with the hollow circles indicates the free hydrochloric acid; the solid line with the solid circles, the total acid, and the broken line with the solid circles, the combined chlorine.

shown in figure 10, there was no essential alteration in the character of the curves in response to the test meal whether the alkalis on the distal side of the pylorus were present or absent. There was the same preliminary rise in the total acid and combined chlorine curves. Subsequently, there was the same increase in the free acid value followed by a decrease to the point of complete neutralization. This final drop in the free acid value was accompanied by a terminal rise in the combined neutral chlorine value whether the duodenal alkalis were present or absent (fig. 10). This procedure was associated with the production of ulcers in the anastomosed jejunum, as occurred in all the experiments with the original type of duodenal drainage operation.

In the second procedure, using the original type of surgical duodenal drainage, fractional gastric analysis showed that the operative procedure had established an impediment to normal emptying. The essential character of the curves was the same before and after operation. The post-operative studies, however, revealed marked retention of the acid chyme in the stomach at the end of the cycle. In the normal dog the stomach was completely empty shortly after the appearance of free acid. During the period when free hydrochloric acid was present, decreasing quantities of juice, from 30 to 5 cc., were aspirated every fifteen minutes until neutralization was attained. After this type of operation, the stomach remained distended with fluid for a prolonged period, 230 cc. of acid chyme being drawn off late in the free acid period in one instance (fig. 11). After this procedure, Morton observed the change of acute traumatic lesions of the gastric mucosa into chronic peptic ulcers. As

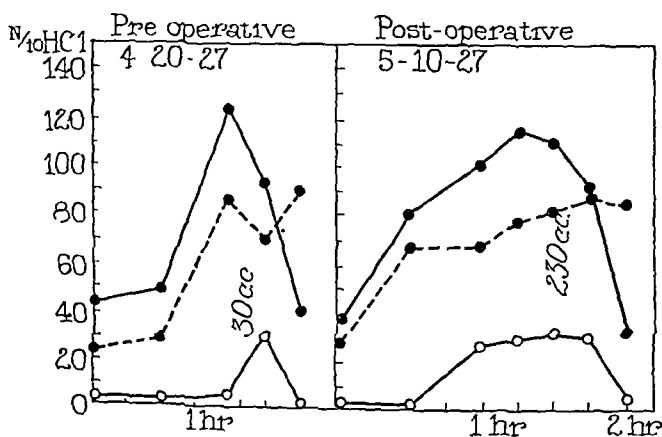


Fig. 11.—Duodenal drainage, late retention of chyme with anastomosis performed at the pylorus, with consequent prolonged exposure of traumatic lesions to normal acid peptic activity.

traumatic lesions healed in the normal dog, the formation of these ulcers was associated with prolonged exposure of the lesion to normal acid chyme.

In the third procedure the alkaline secretions of the duodenum were drained back into the fundic portion of the stomach, as described in the preceding study; the usual types of peptic ulcers were formed in the anastomosed jejunum in a high percentage of experiments. The results of the fractional studies in this procedure are significant as they show the persistence of acid peptic activity after the introduction of duodenal alkalis into the stomach.

Postoperative fractional test meals on three dogs revealed the usual characteristic curves of normal digestion, with average normal values

for free acid at the end of the period; namely, values of from 20 to 30 expressed in terms of cubic centimeters of tenth-normal sodium hydroxide. Figure 12 shows the same preliminary rise in the value of the total acids and neutral chlorides, followed by the usual type of curve for free acid. There was the terminal rise in the value of the neutral chlorine in both instances, before and after operation.

Two other phenomena were observed which may have some influence on the development of these ulcers. One was the elevation of the rate of the basal secretion of acid, and the other, the influence of hemorrhage on secretion.

Basal Secretion of Acid.—During the period when the dogs were eating poorly and they had lost considerable weight, presumably the stage of ulcer development, an increased quantity of the resting basal

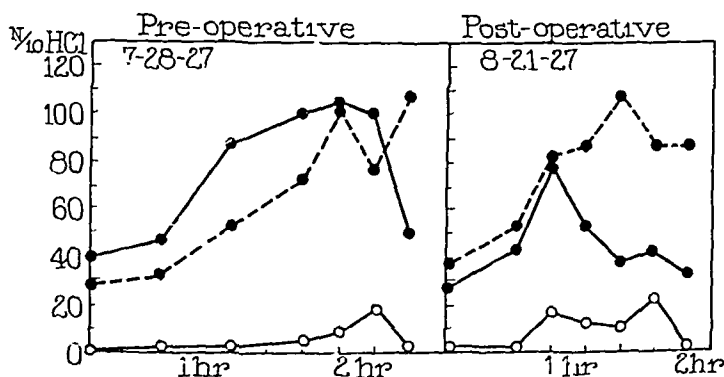


Fig. 12.—Perforated ulcer; the same character of curves was observed before and after surgical drainage of duodenal alkalis (gastric) into the fundic portion of the stomach.

secretion developed suddenly. The usual response to the test meal was observed, but following the completion of the digestive cycle a continuous secretion of juice of considerable acidity persisted (fig. 13). This change was not related in any way to a disturbance of the duodenal secretions because it was observed in dogs in which the alkalis drained into the distal part of the ileum, in those in which the alkalis were drained back into the stomach, and also in those in which gastrojejunostomy has been performed. This increased secretion was induced in a normal dog by a fast of seventy-two hours. It is probable that the phenomenon is related to this normal physiologic response to food after a prolonged fast, in which a high basal secretion is continued long after the digestion of a meal is complete.

Hemorrhage.—The other phenomenon was the association of hemorrhage with high acidity. Blood was aspirated from the stomach of three

dogs. In the first dog there was an absence of acid during a study of the stomach while fasting, and suddenly blood was present as the result of trauma. Immediately afterward, acid of considerable concentration appeared (50 tenth-normal hydrochloric acid). From a second dog 30 cc. of coffee ground material was obtained on a single aspiration of the stomach while fasting, with a free acid value of 60 tenth-normal

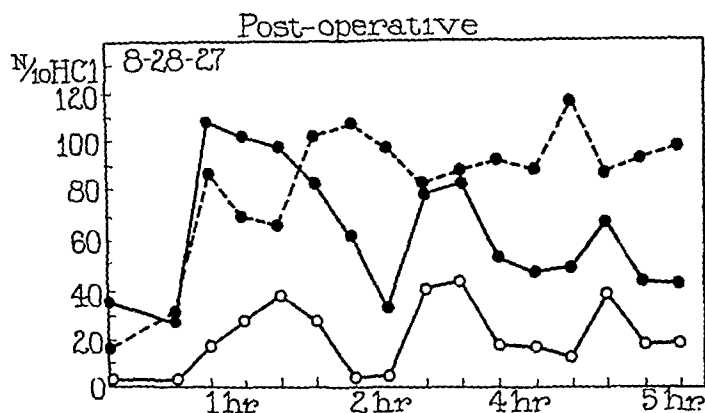


Fig. 13.—Duodenal drainage; continuous secretion of free acid after the completion of the normal response to a test meal (at two hour point) in a cachectic, ulcer-bearing dog.

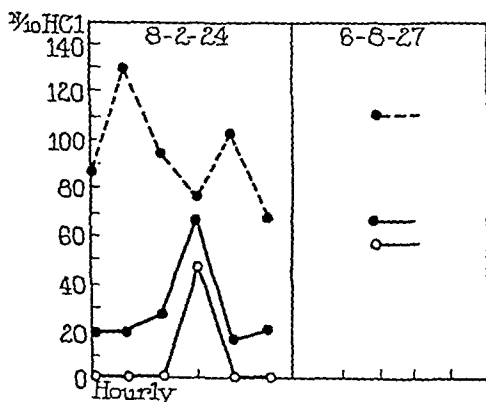


Fig. 14.—Hemorrhage (isolated); first specimen: single appearance of blood and free acid during a course of hourly aspirations; second specimen: single aspiration of coffee ground contents of high acid value.

hydrochloric acid (fig. 14). In a third dog continuous bleeding occurred for the major portion of a twenty-four hour period of fast. There was a definite relationship between the appearance and disappearance of blood and the concentration of the free acid of the gastric contents (fig. 15). It is difficult to judge how much a high basal rate of secre-

tion, as mentioned, may have been responsible for this continuous secretion, but the three observations suggest strongly that blood may act as an adequate stimulus to the secretion of hydrochloric acid.

COMMENT

These studies show that in all the procedures used to produce experimental ulcers, the chemical characteristics of the gastric contents are unaltered. Whether the duodenal secretions beyond the pylorus are partially or wholly removed, or whether they are shunted from the duodenal to the gastric side of the pylorus, the concentration of the acid of the chyme that passes the pylorus remains constant. Consequently, all these ulcers have occurred with the passage of chyme of normal acidity by the pylorus into a segment of intestine where their action is not

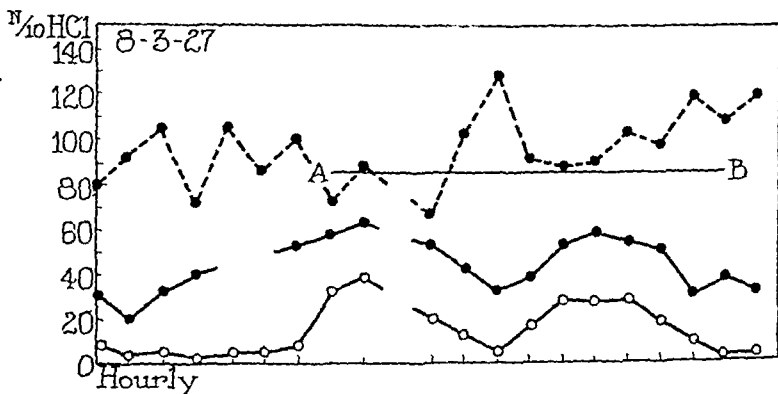


Fig. 15.—Continuous presence of blood in gastric contents aspirated hourly, from A to B, associated with persistent free acid.

terminated by the duodenal alkalis normally present on the distal side of the pylorus.

This constancy of the chemical constituents of the gastric contents, whatever the degree of disturbance of the alkaline factors on the distal side of the pylorus, is not in accordance with Boldyreff's theory of the control of gastric acidity by regurgitation of these alkalis. Whether part or all of the duodenal secretions are eliminated, there is no tendency toward a condition of hyperacidity in the stomach. There is the same adequate control of the acidity of the gastric juice, without evidence of a compensatory mechanism. Hence it would appear that there is a mechanism for the control of the acidity which is entirely intragastric and wholly independent of the regurgitation of duodenal alkalis back into the stomach, and that these experimental ulcers have resulted from the acid peptic activity of normal chyme which was not terminated beyond the pylorus because of the absence of neutralizing alkalis.

As established by the results in the first procedure, the ulcers which developed beyond the pylorus in a moderate percentage of instances following ligation or transplantation of the bile or pancreatic ducts singly, partial hepatectomy and Eck fistulas are dependent on the action of normal gastric chyme, and a partial deficit of the duodenal juices. These ulcers have been produced in a much higher percentage of experiments by establishing a complete deficit of the alkalis beyond the pylorus following transplantation of both ducts, or by doing surgical duodenal drainage. With a gradually increasing acid peptic activity beyond the pylorus, due to the constancy of the chemistry of digestion and the decreasing amount of alkali beyond the pylorus from these procedures, there is a directly increasing tendency to the formation of ulcers. In other words, there appears to be a graded tendency toward the formation of ulcer, directly proportionate to the alkali deficit beyond the pylorus.

Seeking a possible clinical application of these purely experimental facts, it is interesting to speculate whether clinically: (1) duodenal ulcers might result from a deficit of alkali on the distal side of the pylorus associated with disease of the liver, pancreas or gallbladder, which allows the acid peptic activity of the chyme to be sufficiently uncontrolled so as to ulcerate the duodenal mucosa; (2) hypersecretion and hyperacidity of juice of 95 tenth-normal hydrochloric acid might be uncontrolled by the normal quantity of alkaline secretions in the duodenum and thus produce ulcers, or (3) the immunity of the mucosa of the first portion of the duodenum can be lowered by such a mechanism as the toxins of a burn, or the localization of streptococci, so that it becomes susceptible to the degree of acid peptic activity which persists normally in the first portion of the duodenum before the chyme is completely neutralized by the alkalis of the duodenum, and is ulcerated by it.

In the second procedure an extraneous factor has been introduced, whether from nerve injury or from some degree of stenosis of the pylorus associated with end-to-end anastomosis. This factor acts as an impediment to normal emptying. Consequently, the mucosa of the stomach is exposed to normal acid peptic activity for a prolonged period. This fact establishes the basis of Morton's experimental gastric ulcers. He showed that traumatic lesions of the gastric mucosa, which healed rapidly in the normal dog, tended to develop into chronic gastric ulcers after surgical duodenal drainage. He also observed by roentgenologic study that there was slight gastric stasis during the first two weeks, and that this subsequently increased. These fractional test meal studies have shown that whereas traumatic lesions of the gastric mucosa tend to heal readily when exposed to normal acid peptic activity for a normal period, when exposed to normal acid peptic activity for a prolonged period as a result of stasis they tend to change to chronic peptic ulcers. Since the

only demonstrable variable following this operation is this prolonged exposure of the lesion to normal acid peptic activity, it is probable that the destructive activity of acid pepsin over a long period was responsible for the development of these gastric ulcers. This concept is in accord with Hughson's conclusions when he showed, after a series of roentgenologic studies on the emptying of the stomach, that in animals in which delay is demonstrated ulcerations remain active at least twice as long as in the group in which emptying is more rapid.

The demonstration that experimental gastric ulcers are associated with prolonged exposure to the normal acid chyme suggests hypothetical conditions that might lead to the development of gastric ulcers in clinical cases. A traumatic lesion of the gastric mucosa, associated with pylorospasm and prolonged retention of the fluid chyme of normal digestion, might result in a gastric ulcer. With lowered immunity of the gastric mucosa, for a prolonged period of time, by such an agent as the localization of streptococci, the normal acid peptic activity of digestion, together with the mechanical factors of the region, might initiate a lesion and produce a chronic peptic ulcer.

The persistence of normal values for acid in the third procedure, despite the drainage of all the duodenal alkalis into the fundic portion of the stomach, is an unexpected observation which may possibly be explained by an increase in the amount of acid secreted, to compensate for these alkaline juices. Whatever the explanation, the question is raised as to whether the favorable results following gastro-enterostomy for clinical ulcers may be due not so much to the neutralizing effect of these juices as to the mechanical drainage of the free acid aliquot which terminates the digestive cycle. It may be that, with the relaxed state of the musculature at the end of digestion, all the final free acid which usually coincides with the period of distress may drain through the relaxed stoma and thus spare the ulcer from its destructive action. This result supports the idea that normal acid pepsin, acting in the absence of an effective neutralizing mechanism, is the probable cause of these experimental ulcers. They are not due to the loss of any specific protective activity of the juices other than chemical, because, in this third procedure, all the duodenal alkalis are present at a point proximal to the site of ulcer formation where they do not alter the normal chemistry of digestion, and are displaced only from the point of effective neutralization in the duodenum.

Experimental data support the clinical impression that hemorrhage may stimulate the secretion of an amount of acid that will have a deleterious effect on an ulcer. Likewise, a high rate of basal secretion of acid may develop which will be equally harmful to an ulcer.

Since it has been shown that normal acid peptic activity is the chemical factor associated with the production of these experimental ulcers,

one fact is revealed which is of major clinical significance: the graded immunity of the upper intestinal tract to the destructive action of the gastric juice, or, conversely, the increasing vulnerability of the mucosa to the formation of ulcer as the distance from the cardia of the stomach increases.

Under the mechanical conditions of these experiments the gastric mucosa did not ulcerate from exposure to the normal autolytic action of the juice for normal periods of time. Even traumatic lesions in all parts of the mucosa healed when exposed to acid pepsin for the normal periods of digestion. Furthermore, the inherent immunity of the mucosa to this action is so marked that it never ulcerated spontaneously from prolonged exposure to this activity as resulted from surgical duodenal drainage. Even with prolonged exposure to this autolytic activity after surgical duodenal drainage traumatic lesions in the cardia healed successfully. Similar lesions in the prepyloric segment, which is the site of clinical formation of ulcer, developed into chronic ulcers from this prolonged exposure; but here there are also mechanical factors involved which tend to prevent the healing of such lesions.

The duodenal mucosa ulcerated spontaneously from exposure to unneutralized acid chyme of normal digestion (in the absence of alkalis after surgical duodenal drainage) in a fair percentage of experiments. The jejunal mucosa ulcerated in practically all instances when exposed to this activity under the same experimental conditions. The contrast between the immunity of the gastric mucosa and the susceptibility of the duodenal mucosa to spontaneous ulceration probably explains the clinical preponderance of duodenal over gastric ulcers in a ratio of four to one, provided the initial lesion is established as frequently in the stomach as in the duodenum. This gradient of immunity would also explain the tendency for gastrojejunal ulcers to form in the relatively unfavorable environment of gastrojejunostomy, the low percentage of occurrence being dependent on unrecognized factors.

It is not necessary to postulate a state of hyperacidity to explain the formation of chronic ulcers. They have resulted experimentally from exposure to normal acid pepsin for the remarkably short periods of normal digestion, under proper experimental conditions. It is probable that, since meat is progressively disintegrated to a fluid state by acid in combined form during early digestion, the devitalized cells of an ulcerating lesion may be somewhat susceptible to the action of this combined acid and pepsin of early digestion. Probably the action is not so marked as from the free uncombined acid of late digestion.

SUMMARY OF STUDY II

In a long series of experimental studies, Mann and his co-workers have produced typical peptic ulcers by injuring the neutralizing mechanism in the duodenum, so that the acid chyme from the stomach

could act on the mucosa without hindrance. In earlier studies I found that the mechanical factors active in producing these ulcers, and presumably influencing clinical ulcers, were the force of the stream ejected through the pylorus, the friction of coarse cellulose food and the vigorous motor activity of the prepyloric segment.

Using a method of fractional gastric analysis which I devised for use on the dog, the underlying chemical factor in the production of these ulcers was shown to be normal acid peptic activity. The ulcers produced exhibit the highly destructive character of the gastric chyme. Of great significance is the gradient of immunity of the mucosa of the intestinal tract to ulceration, which probably is the deciding factor in determining the greater frequency of duodenal ulcer as compared to gastric ulcer, and the tendency for jejunal ulcer to develop following gastro-enterostomy.

These studies demonstrate that the gastric mucosa possesses considerable immunity to the autolytic activity of the acid and pepsin secreted by the stomach, whether exposed to it for a normal period or for a prolonged period, because spontaneous experimental ulcers of the chronic type produced in these experiments never developed in the stomach. Likewise, the normal duodenal mucosa is completely immune to this activity under the condition of a normal relationship between the acid chyme ejected through the pylorus and the neutralizing secretions present in the duodenum.

With slight disturbances of the interrelationship of normal functions in the pyloric region, the ordinary factors active in this segment assume pathologic significance. By experimentally disturbing these relationships, a considerable body of evidence has been developed which stands in answer to Cohnheim's statement that the real difficulty is in determining "the unknown something which prevents the healing of ulcer." The evidence indicates that the "unknown something" may be the normal acid peptic activity of the gastric chyme with the mechanics of the region, which act as a definite handicap once a lesion has been established.

III. AUTOLYSIS OF THE STOMACH

Gastromalacia, or self-digestion of the stomach, is a phenomenon, the occurrence of which during life has been much disputed by pathologists. If the occurrence of autodigestion were possible, one might consider it related to the formation of ulcer so far as one would represent a generalized and the other a localized digestive process. In either case the process could be attributed to an abnormal activity of the digestive enzymes, or to a deficiency of the tissues for natural self-protection against enzymatic activity. That there is such a relationship between autolysis and the formation of ulcer is suggested by the possible occurrence, as reported here, of generalized autolysis of the stomach following surgical drainage of the duodenal juices back into the stomach: the

procedure which resulted in the formation of ulcer. Because of this probable relationship, a brief review of general autolysis and of the resistance of living tissue to gastric digestion is relevant.

The literature contains few references to intra vitam autolysis of the stomach. Its occurrence after death has long been appreciated by pathologists. If an animal is killed at the height of digestion and kept warm, digestion of its stomach and adjacent tissues will take place. Virchow, Elasser and Cohnheim agreed that this was always a cadaverous process. Rokitsansky maintained, however, that it occurred during life, particularly in the end-stages of extensive tumors of the brain. Cases reported from Ziemssen's clinic by Mayer and Leube seem to bear out this contention. The mechanism of protection against autolysis has long been a source of speculation and study. Stah believed that the stomach was protected from autolysis by the sensitive soul; John Hunter¹²⁸ and Spallanzani believed that the vital power protected the body by some inherent energy. Bernard¹²⁹ was the first to view the problem in a physiologic manner, when he attributed this immunity to the fact that pepsin was not absorbed by the gastric mucosa (probably because of the mucous coat), and because any destroyed cells were rapidly regenerated. Harley ascribed the protection to the mucous film, and Pavy to the alkalinity of the blood, which neutralized the acid.

I found only one report of experimental gastric autolysis in the literature. Frouin¹³⁰ observed it while studying an isolated stomach with a fistula to the anterior abdominal wall. After transacting the cardia and pylorus, he anastomosed the esophagus and duodenum, so that the continuity of the digestive tract (with the stomach excluded) was reestablished. He closed the two ends of the stomach, and established a fistula to the anterior abdominal wall. Besides this surgical fistula, another smaller one formed accidentally between the cardia of the stomach and the esophagus. Through this fistula small quantities of food seeped into the stomach and were retained. The animal died on the twenty-ninth day, and necropsy was done within two hours. Almost complete digestion of the gastric mucosa had occurred. Frouin believed this resulted from stagnation of the products of protein digestion and gastric secretion. He repeated the study on an isolated stomach, administering salt to increase gastric secretion and injecting peptone into the stomach. Hemorrhage into the stomach resulted, which he assumed

128. Hunter, quoted by Turck: *J. A. M. A.* **46**:1753 (June 9) 1906.

129. Bernard, Claude, quoted by Dragstedt and Vaughan: *Arch. Surg.* **8**:791 (May) 1924.

130. Frouin, Albert: Des causes de la résistance de l'estomac à l'auto-digestion, *Compt. rend. Soc. de biol.* **52**:749, 1900; Auto-digestion expérimentale de l'estomac, *Presse méd.* **16**:769, 1908; Résistance de l'estomac à l'auto-digestion, *La pathogénie de l'ulcère*, *ibid.*, p. 809.

would have resulted in autolysis if repeated often enough. In my study two cases of autolysis followed drainage of the duodenal juices back into the stomach, which caused an unbalanced intermixture of the digestive juices. In analyzing this phenomenon, the causative factors may be attributed to one of two factors: to increased enzymatic activity associated with prolonged retention of digestive juices which results from the procedure, or to deficiency in the normal protective mechanism of the mucosa.

The enzymatic activity of the digestive juices is analogous to the general autolytic or enzymatic activity elsewhere in the body. The analogy is similar to that existing between the endotoxins and ectotoxins of bacteria. Corresponding to endotoxins the tissues contain peptic, tryptic and ereptic-like enzymes which are active within the cell in metabolism, disease, involutional changes and death. Turck,³⁹ Effront and Robertson showed that these proteolytic intracellular enzymes belong to the same group as the digestive ferments. Analogous to bacterial ectotoxins are the enzymes of the gastro-intestinal tract, active outside the cell body, ordinarily inhibited from attacking the living mucosa, but reported in this paper to have possibly done so.

The first realization that the most constant tendency of tissue is toward spontaneous disintegration came, according to Levene,¹³¹ when Manassein and Buchner¹³² demonstrated a single substance in the cell which led to fermentation after the cell was crushed and dead. Salkowski¹³³ recognized that disintegration of liver, muscle and suprarenal gland was due to enzyme activity, and called the process "auto-digestion"; in 1900, Jacobi,¹³⁴ introduced the name "autolysis." An appreciation of the universality of this process soon followed. Mueller³⁶ showed that resolution in pneumonia was by autolysis, and Opie that the exudate was absorbed by the proteolytic activity of leukocytes. That pathologic processes represent only an intensified picture of normal protein metabolism by enzyme activity was first suggested by Dochez.¹³⁵ Flexner noted the intense self-digesting tendency in the organs of those who succumbed to typhoid and other infectious diseases. This process also occurs during life, in phosphorous poisoning, acute yellow atrophy, atrophy of the thymus gland, involution of the uterus and softening of tumors. Sykes and Meyers asserted that autolysis is a normal metabolic activity, for during a prolonged fast the amino-acid content of the blood

131. Levene, P. A.: Autolysis, The Harvey Lectures, 1905-1906, p. 73.

132. Manassein and Buchner, quoted by Levene: Autolysis, The Harvey Lectures, 1905-1906.

133. Salkowski, quoted by Dochez: J. Exper. Med. **12**:666, 1910.

134. Jacobi, Y., quoted by Dernby: J. Biol. Chem. **35**:179, 1918.

135. Dochez, A. R.: Intracellular Proteolytic Enzymes of Liver. J. Exper. Med. **12**:666, 1910.

is maintained by autolysis of muscle protein. Notwithstanding the presence of destructive enzymes in all tissues, however, the organs succeed in guarding their integrity, as does the stomach, from enzyme activity. It is only when there is an exaggeration of the normal process, or a disturbance in the normal relationships which keep autolysis within bounds, that self-digestion ensues.

Bile may play a part in this process of gastric autolysis, as indicated by Tatum.¹³⁶ He cut blocks of various tissues and incubated them in fresh bile for from two to four hours at 30 C. They were sectioned and stained, and autolysis of the peripheral margins was found, with pyknotic nuclei which had lost their staining capacity for hematoxylin. No such effect was shown in dead tissue subjected to the same process. The action was accelerated by acid, but was inhibited by blood serum and alkali. In an effort to determine the constituent of the bile responsible for this phenomenon, he studied the effect of sodium glycocholate which he found less penetrating than either taurocholate or mucin-free bile, both of which had equal influence in causing the change. Unaltered bile was most penetrating. Boiling did not affect its influence, but animal charcoal diminished it. Bradley and Taylor¹³⁷ criticized this work because histologic changes were interpreted in terms of chemical action. They attributed the results to the solvent action of bile salts on the cell lipoids, claiming that the picture was that of cytolysis and not one of enzyme activity.

One of the possible variants that is of major importance in autolysis is the hydrogen ion concentration; this has been recognized as a controlling factor. Hedin,¹³⁸ among the earliest investigators, reported increased autolysis in an acid medium and decreased activity in an alkaline medium; he also reported that if the action is started in acid first and then transferred to alkali the autolysis is more complete than if acid acted alone. Morse¹³⁹ considered that autolysis is an autocatalytic reaction due to spontaneous increase in the hydrogen ion concentration. Bradley believes that the increase in the hydrogen ion concentration alters the proteins into forms more readily digested by enzyme activity. Dernby¹⁴⁰

136. Tatum, A. L.: The Influence of Bile on Autolysis, *J. Biol. Chem.* **27**:243, 1916.

137. Taylor, F. J.: Duodenal Ulcer in the Dog, *Vet. J.* **78**:343, 1922. Bradley, H. C.: Autolysis and Atrophy, *Physiol. Rev.* **2**:415, 1922; Studies on Autolysis: VIII. The Nature of the Autolytic Enzymes, *J. Biol. Chem.* **52**:467, 1922. Bradley, H. C., and Taylor, F. J.: Studies on Autolysis: V. The Influence of Bile on Autolysis, *J. Biol. Chem.* **29**:281, 1917.

138. Hedin, quoted by Dernby: *J. Biol. Chem.* **35**:179, 1918.

139. Morse, M.: Enzyme and Reaction of Medium in Autolysis, *J. Biol. Chem.* **30**:197, 1917.

140. Dernby, K. G.: A Study on Autolysis of Animal Tissues, *J. Biol. Chem.* **35**:179, 1918.

found three distinct groups of proteolytic enzymes in the tissues, with end-products identical with those of pepsin, trypsin and erepsin of the gastro-intestinal tract, each acting at a different hydrogen ion concentration. In studying different tissues he found the stomach to contain a large amount of pepsin, with optimal activity in a hydrogen ion concentration range of from 2 to 3. This enzyme was present in all tissues, acting at an optimal hydrogen ion concentration of 3.5 and splitting proteins into peptones, but no farther. Trypsin-like and erepsin-like enzymes were present, acting in an optimal hydrogen ion concentration of 7.8, attacking only peptones and peptides, and yielding amino-acids. Self-decomposition of tissue proceeded best at a hydrogen ion concentration of from 5 to 6, that is, between the optimum for pepsin and trypsin. Bradley criticized Dornby for his use of the terms peptic, tryptic and ereptic enzymes, because he claimed these tissue enzymes have a different optimal hydrogen ion concentration than the digestive ferments. He found that tissue protease is inhibited at a hydrogen ion concentration of 2.6, which is optimal for pepsin, and that pepsin is least active at the optimal hydrogen ion concentration for tissue autolysis. He also found that the addition of trypsin carried the splitting of proteins beyond the point to which autolysis alone could carry it.

Another contribution on the influence of hydrogen ion concentration is the work of Rona and Mislowitzner in which they found that autolysis of the liver of guinea-pigs was maximal with acetate buffers of p_H from 3.5 to 3.8, and with phthalate at p_H 4.2. The action was arrested by changing it briefly to p_H 8. Most of the nitrogen in the autolysate was found in the form of polypeptides with 50 per cent autolysis; if the products of digestion were removed by dialysis, the digestion was increased to 90 per cent. Nagai,¹⁴¹ while studying the pancreatic juice, found that with increased acidity the initial velocity of autolysis was decreased, but that it recovered in a number of hours. He also found that increased alkalinity augmented the initial velocity, but that it soon fell, indicating destruction of the enzyme.

Thus it may be seen that surviving tissue variations in the hydrogen ion concentration can augment the destructive action of proteolytic enzymes. It may be that the abnormal chemical status which the present operative procedure establishes, with fluctuations from acid to alkali, renders the proteolytic enzymes of the digestive tract abnormally active, leading to digestion of the stomach. However, there is another factor that must be considered, that is, the possible impairment of the normal mechanism of protection against the action of these enzymes.

Bernard first demonstrated the power of the digestive juices to disintegrate living tissue by introducing the leg of a frog into a dog's stomach

141. Nagai, Kazuo: On the Autolysis of Pancreatic Juice, *J. Biochem.* 2:399, 1922-1923.

through a fistula and watching the digestion of it. Pavy found this to be true also of a rabbit's ear. He believed that in the wall of the stomach the alkalinity of the blood neutralized the hydrochloric acid. Schiff⁹² demonstrated that the mucous layer protects the stomach from pepsin by showing that the mucus which forms over the orifice of a canula placed in a gastric fistula will allow the passage of hydrochloric acid, but not of pepsin. De Klug,¹⁴² seeking to verify this protective rôle of mucus, made a powdery extract of intestinal mucosa which had all the characteristics of mucin; it inhibited the action of both pepsin and trypsin even when heated. The same inhibiting effect was demonstrated with mucus from bile, and with pseudomucin from an ovarian cyst. Palier¹⁴³ believed that the stomach did not digest itself because the mucus and peristalsis of the tract constantly repelled the digestive juices from the wall.

Weinland attributed this immunity to an antiferment contained in the gastric mucosa. Katzenstein stopped the digestion of spleen and living intestine by adding an extract of gastric mucosa to the gastric juice. Lecine and Hatz found that a fragment of gastric mucosa inhibited the digestion of egg white, which was not true of intestinal mucosa. Kawamura, studying this antiferment, took equal sized pieces of gastric mucosa, intestinal mucosa and spleen and added each to digesting gastric juice according to Katzenstein's conditions. The stomach slightly inhibited digestion, the intestine somewhat more and the spleen most of all. Blood serum also exercised a decided inhibitory effect on digestion. He concluded that there is an antipepsin in the blood, demonstrable in the gastric mucosa and other tissues, and that ulcer arises from a circulatory disturbance resulting in a lack of antipepsin in a circumscribed area of the stomach. All of these observers considered autolysis as due to a break in the equilibrium between enzyme and anti-enzyme, predisposed to by vascular changes and by traumatic and nervous lesions. Lieblin, studying the quantitative value of antipepsin in the blood, found it fairly constant in healthy and sick persons, but in cases of gastric ulcer it was inconstant, sometimes high and sometimes low.

Surgical procedures have been used to study this immunity of living tissue to digestion. Katzenstein introduced a loop in intestine into the stomach of a dog, and death resulted in eight days from digestion of the loop. He obtained the same result with a rat. He then anastomosed a resected segment of intestine at two points on the greater curvature, so that the gastric juice passed through it as a collateral canal. After several days the dog died with necrosis and digestion of the mucosa of

142. De Klug, Ferdinand: Pourquoi les ferments protéolytiques ne digèrent-ils pas l'estomac et l'intestin sur le vivant? *Arch. internat. d. physiol.* 5:297, 1907.

143. Palier, E.: *Etiology of Gastroduodenal Ulcer*, New York M. J. 117:659, 1923.

the implanted segment. The peritoneal surface of a loop of duodenum was implanted into an opening made in the pyloric antrum. This resisted digestion. Implanted spleen and omentum were promptly digested. Katzenstein concluded that the gastric mucosa contained antiferments which were not present in the intestinal mucosa. Lecine and Hatz, on the contrary, found that when great care was taken not to injure the blood supply, the spleen and loops of intestine could be implanted into the stomach without undergoing digestion. They concluded that a tissue which secreted a juice was protected from its action. Stewart suggested that various body membranes have developed a specific resistance to the fluids with which they normally come in contact, but not to other juices. Matthes believed that the gastric mucosa had developed a special resistance to hydrochloric acid, which he claimed was destructive to other tissues.

Dragstedt and Vaughan⁷⁰ transplanted flaps of the lower part of the duodenum, and of the upper part of the jejunum, ileum and colon into the pyloric region with the blood supply intact, and the transplant had not digested at the end of three months. If these patches were sutured with the serosa toward the lumen, the serosa and the muscularis were digested, but the mucosa remained resistant. A split spleen was implanted with its raw surface toward the lumen. It was not digested even though it did not have a mucous coat; also, epithelium grew inward covering its edges. This, it was claimed, ruled out any protective function by the mucous coat, and emphasized the intrinsic resistance of the naked exposed living cell to digestion. Kawamura, using dogs, exposed parts of the stomach, intestinal wall and spleen to the action of gastric juice, but they were not affected while the circulation was unimpaired. Only after necrosis had begun as a result of circulatory disturbance was there any sign of digestion. As mentioned, de Takats and Mann, and later Morton, transplanted jejunal patches into the wall of the stomach. With the exception of one condition, they resisted digestion until after duodenal drainage had been established, which probably resulted in delayed emptying of the chyme and, consequently, prolonged exposure to the acid chyme. Mann also transplanted loops of jejunum into the posterior wall of the stomach. These remained normal until the extirpation of the suprarenal glands, following which autolysis ensued.

METHOD

This study presents two instances of autolysis of the gastric mucosa. The phenomenon was unexpected and was observed after an operative procedure in the study of experimental peptic ulcer.

The operation consisted in draining the duodenal secretions back into the fundic portion of the stomach. The pylorus was severed, and the duodenal end was inverted. The jejunum was severed just distal to the ligament of Treitz.

The distal end was brought up and anastomosed to the open gastric end of the pylorus, thus reestablishing the continuity of the tract, with the duodenum excluded. The distal end of the isolated duodenum was anastomosed to the fundic portion of the stomach, so that the alkaline secretions were drained into that portion of the stomach (fig. 1).

In three of the dogs an effort was made to influence the autolytic process by the administration of different salts contained in capsules. Five grams of sodium chloride was administered to one dog three times a day. This was done because Frouin had administered the salt, and believed that it had increased the tendency to autolysis. To a second dog, 5 Gm. of sodium bicarbonate was given three times a day, on the chance that the process might be initiated by shifting the hydrogen ion concentration, even momentarily, to the alkaline side of neutrality. To a third dog, 5 Gm. of sodium taurocholate was given three times a day with the purpose of augmenting the action of the bile which was completely drained into the fundus of the stomach. Rywosch had produced inflammation and gangrene of the stomach of rabbits by feeding an excess of bile salts. The administration of the salts was continued over a period of a month, but in none of the three dogs did autolysis of the gastric mucosa develop.

RESULTS

Two of twenty-six dogs subjected to the foregoing operative procedure died suddenly. Necropsy revealed extensive autolysis of the gastric mucosa. The first dog died twenty-three days after operation, during which period it had lost 1.8 Kg. At necropsy, both lungs were collapsed and the pleural cavities contained a considerable amount of thin chocolate-colored fluid which was strongly acid. The mediastinum had been entirely eaten away, except for the main blood vessels, the trachea and the lower part of the esophagus. The upper and intrathoracic portions of the esophagus had been entirely eaten away. This explained the fluid in the chest, which, being strongly acid, was probably gastric juice. The digestion had extended through the structures of the neck, and the upper limit was determined by the lower part of the skull. The whole hand could be inserted into the cavity in the neck. The peritoneum was clean and relatively free from adhesions. The stomach had undergone considerable digestion at the points adjacent to the stoma and to the delivery of the duodenal contents. The digestion had entirely destroyed the mucosa, leaving the submucosal vessels standing by themselves. The stomach contained coffee ground material. All anastomoses were satisfactory.

The second dog died five months after operation; it lost 1 Kg. Necropsy revealed autolysis of the stomach and jejunum, and ulcer formation. The peritoneum was clean, and all suture lines were intact. The walls of the stomach appeared thin and transparent as the organ was washed with water. When opened, extensive autolysis of the gastric mucosa was found. Over an area approximately 10 by 7 cm., the cardia was denuded of mucosa, and the glistening submucosa formed the inner lining of the stomach. An area of jejunum close to the anastomosis,

about 2 cm. in width and extending about 5 cm. in a longitudinal direction, was likewise denuded of mucosa. In the center of this autolyzed area, two perforated ulcers were found (fig. 16). The relationship of the autolyzed surface and the ulcers suggested a possible identity between the mechanism that leads to a localized area of destruction, as an ulcer, and that which leads to extensive autolysis of the gastric mucosa.

COMMENT

It is impossible to estimate the significance of the results. They are isolated phenomena in an uncontrolled experiment. It is not possible to judge how much of the process is *intra vitam* and how much is post-mortem change. It is significant, however, that autolysis occurred in



Fig. 16.—Extensive area of autolysis of the mucosa, *a*, of the stomach and jejunum, associated with the formation of perforated ulcers, in an experimental study in which the duodenal alkalis were drained back into the fundic portion of the stomach.

two animals subjected to the same operative procedure, and that they were isolated specimens in a large group of normal and experimental animals all receiving the same kennel care. Shortly after death, all animals were placed in refrigeration. Routine careful investigation of all organs was carried out, and never was this phenomenon observed. It seems fair to assume that the operative procedure established conditions that were conducive to the initiation of the autolytic process.

Conclusions cannot be drawn concerning the relationship of this process to that of general tissue autolysis. In both instances comparable enzymes are active, in the one instance within the cell and in the other instance outside the cell. General autolysis is definitely influenced by

shifts in the hydrogen ion concentration of the environment, and in these instances of autolysis of the mucosa of the stomach there is the possibility of a widely shifting hydrogen ion concentration. It is interesting to speculate whether the conditions of the experiment made it possible for the intragastric enzymes to attack the gastric mucosa. If this is true, it is possible that an ulcer may represent a similar process limited to an area of lowered resistance.

Why does not the stomach digest itself ordinarily? What is the source of protection against this destructive process? This seems to be a problem more open to theory than to exact investigation. In a series of studies which I made on the control of the acidity of the gastric juice, it seemed that in the active state of digestion food combined readily with the acid, and that after the completion of digestion the residual free acid was emptied from the stomach. It appeared that in the resting state the rate of secretion was lowered to a level at which, according to Foster's evidence, it may be combined with the mucus in the presence of pepsin at body temperature. This reaction may take place immediately in the lumina of the glands in the fundus. The gastric mucosa would probably be protected from any residual free acid in the lumen of the stomach by a coating of this mucus capable of combining with the acid.

SUMMARY OF STUDY III

The literature contains little on autolysis of the stomach. Two such instances, observed in an experimental study, are reported. There may be a general analogy between intracellular enzymatic activity responsible for general autolysis and the extracellular enzymatic activity responsible for the instances of autolysis of the gastric mucosa. This process may represent the mechanism by which isolated ulcers of the mucosa are established, when there is local reduction in the immunity of the mucosa to this autolytic activity. It is probable that the mucous secretion of the stomach by virtue of its capacity to combine with free acid forms the principal defense of the gastric mucosa against autolysis.

LOOSE CARTILAGE FROM INTERVERTEBRAL DISK SIMULATING TUMOR OF THE SPINAL CORD*

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BALTIMORE

The two loose cartilages here reported were disclosed at operation for presumed tumors of the cauda equina. In each instance the spinal canal was completely blocked as shown by the shadows of iodized oil 40 per cent (figs. 1 and 2). The signs and symptoms were so rapidly progressive and the pain in the spinal column so severe that presumptive diagnoses of carcinoma of the vertebra were made. The fact that the two cases appeared only a few months apart leads me to believe that the lesion may not be so infrequent, although a review of the literature has failed to disclose other cases of their kind. The lesion is a completely detached fragment of cartilage from an intervertebral (lumbar) disk and is surrounded by serum. It bulges dorsally into the spinal canal as a tumor, and by compressing the roots of the cauda equina causes motor and sensory paralysis, loss of reflexes and of rectal and vesical control. The lesion is undoubtedly of traumatic origin.

REPORT OF CASES

CASE 1.—A sparsely nourished man, aged 47, was referred by Dr. Lewellys F. Barker. Whether or not the past history was relevant to the present illness was not clear at the time. Three years earlier a tumor had been removed from the hand; a microscopic diagnosis of a sarcoma was made. The scar on the hand, the regions of the epitrochlear and axillary glands, had since been treated intensively with radium. Subsequently an axillary gland was removed, but no sign of malignancy was discovered. Two years later, he consulted Dr. Barker because of convulsions which dated back two years.

The patient was readmitted to Dr. Barker's service on May 15, 1928, with an entirely different complaint. Ten weeks before admission he had a severe attack of pain in the lumbar region and both hips; there was more pain in the right hip. The pain radiated down the back of both legs, with more pain in the right leg. After two months of excruciating pain, it was necessary to resort to morphine for relief. Six weeks before admission to the hospital, a "dead feeling" developed in both legs and gradually increased. Two weeks before, he was barely able to stand alone. Assistance was necessary to walk a short distance. One week before, retention of urine and feces developed; after that time he was catheterized twice daily. He lost 42 pounds (19.1 Kg.) in weight, 15 pounds (6.8 Kg.) of which were lost in the last two months before admission. Pain in the lumbar region, hips and legs steadily became more severe.

On admission to the Johns Hopkins Hospital, the patient was found to have a total flaccid paralysis below the knees. Except for feeble flexion and extension

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* From the Johns Hopkins University and Hospital.

of both legs at the hips, the legs were useless. Sensation was impaired though not entirely lost; sharp and dull stimulation were not differentiated. Vibratory sense was lost. Flexion and extension of the toes could not be differentiated, though the patient could tell which toe was touched. There was loss of sphincter control of feces and urine (retention of urine was complete). Marked tenderness, even to light pressure, was noted over the spine of the third and fourth lumbar vertebrae. The lumbar muscles were in continuous strong spasm. Movements of the spine were painful, and even coughing intensified the pain. The patient was averse to any movement, and flexion of the knee was painful.

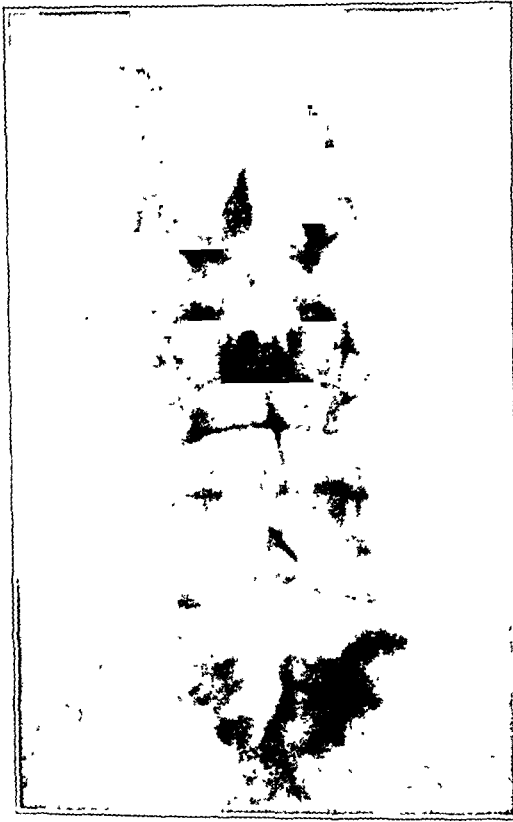


Fig. 1 (case 1).—Shadow of iodized oil at the upper margin of the tumor caused by a loose cartilage of the intervertebral disk.

The abdominal reflexes were normal; the cremasteric reflexes were not obtained, and the knee jerks were subnormal. The Achilles jerks were not obtained, and there was no ankle clonus. The Babinski, Gordon and Oppenheim tests were negative. The Wassermann reaction of the blood was negative. Roentgenograms of the lumbar spine were negative.

Through a cisternal puncture, 0.5 cc. of iodized oil was injected. It stopped abruptly at the level of the third lumbar vertebra.

Preoperative Impression.—The rapidly progressive paralysis, sensory, motor and sphincter, the severe pain and tenderness in the back, the great loss of weight and finally the history of a malignant lesion of the hand (doubtless incorrect) led

me to suspect a metastatic lesion of the third lumbar vertebra, despite the absence of signs of destruction in the roentgenogram.

Operation.—It was decided to explore the lesion to be sure of its character, and if it was malignant to perform a chordotomy. The laminae of the third and fourth lumbar vertebrae were removed. No change in the amount of extradural fat was observed. When the dura was opened, the roots of the cauda equina herniated markedly (fig. 3). The nerves were greatly injected, and because of this increased vascularity, oozing followed when they were touched. It was seen

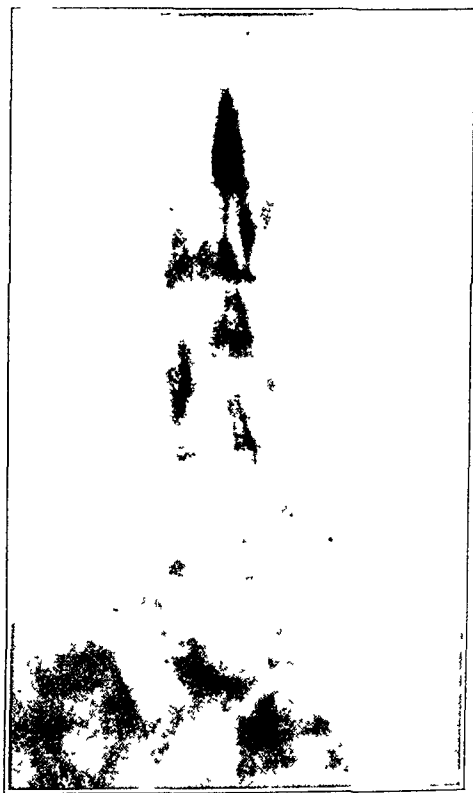


Fig. 2 (case 2).—Iodized oil shadow at the upper margin of the tumor.

that there was a sharp knuckle of the roots protruding backward. Above and below this knuckle, there was a sharp drop. Palpation revealed a hard tumor lying beneath the roots and pushing them through the dural opening. The roots were then retracted to the left, and a bulging tumor mass was seen. It was round, about as large as a big hazelnut (about 1.5 by 1.5 cm.) and entirely covered by dura. It seemed semifluctuant when touched with the point of the forceps. The lesion was still thought to be malignant, even though the ventral dura was intact. After some hesitation I thought it advisable to incise the dura, and much to my surprise a border of loose cartilage protruded through the opening (fig. 4). With forceps, the cartilage was picked up and delivered without resistance. It was roughly oval, but crumpled. When straightened, it measured 2 by 0.8 by 0.3 cm. Its edges



Fig. 3—Drawing showing the roots of the cauda equina bulging backward.



Fig. 4—Cauda equina retracted exposing tumor on ventral surface of the canal. The tumor has been incised and the loose cartilage is being delivered.

were very irregular, almost serrated (fig. 5). It had no attachments to the vertebral cartilage. Exploration of the cavity with a small curet revealed no additional sequestrums either of cartilage or of bone. A few drops of fluid escaped with the "floating cartilage." On gross inspection, there was no evidence of bone.

Microscopic Report.—A few scattered cartilage cells in varying states of degeneration were scattered through a pink-staining hyaline mass which was not entirely homogeneous, but in places was broken up by scattered fibrils longitudinally arranged. There were no inflammatory changes. No round or polymorphonuclear cells appeared in the sections, and there were no bone cells or deposits of calcium.

Postoperative Course.—Recovery from the operation was uneventful. The pain, though immediately relieved, was not at once abolished. Gradually it became less and less, and in a few weeks ceased. Vesical control was regained in two weeks and rectal control four weeks after operation. Return of motor power began seven weeks after the operation (three weeks after leaving the hospital). In a letter written six months after the operation, the patient stated that he could walk long distances without support, and every week improvement continued.

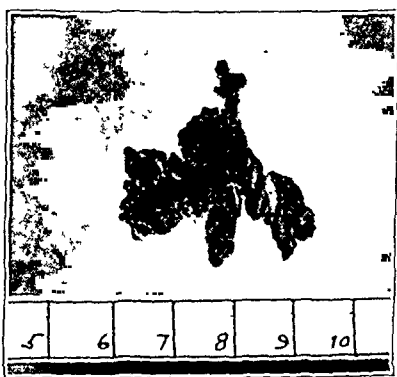


Fig. 5.—Loose cartilage removed from patient in case 1.

Subsequent History.—After the nature of the lesion was known, the recent history was again reviewed for trauma. The patient then recalled a severe, sharp lumbar pain which came with a sudden jolt when he was riding horseback three months before, or about two or three weeks before the onset of his present illness. He had forgotten the pain, since it disappeared after a few hours and had not returned during the succeeding days.

CASE 2.—A large, robust man, aged 61, was referred by Dr. Eugene V. Parsonnet of Newark, N. J., because of paralysis of the lower limbs. He had been in perfect health until twelve weeks before, when he pushed his automobile out of the driveway. Immediately afterward, a dull, heavy pain developed in the small of the back. He went about his duties, and in a few days the pain abated. A week later, without appreciable cause, a sudden excruciating pain struck the lumbar region and radiated down the posterior aspect of both thighs. The pain was so severe that he had to remain in bed for two or three days. Movement of the spine caused severe pains. A few days later, he was again relieved, and returned to work. Ten days after the second attack, he was seized with a third and even more severe pain at the same site and with the same referred distribution.

At this time (about a month after the first pain), he was seen by Dr. Parsonnet, who noted the following: 1. The normal anterior lumbar curve was missing.

2. There were definite scoliosis of the lumbar spine to the right. 3. Marked spasm of the erector spinae muscles. 4. Moderate tenderness at the third and fourth lumbar spinous processes. 5. The right knee jerk was diminished and the right ankle jerk absent. The patient was able to stand, but any movement elicited great pain.

An orthopedic consultant was called who advised stretching the sciatic nerves. This was done under deep anesthesia with ether. A plaster jacket was applied with the back in hyperextension. The spica extended to the toes of the right foot; the left leg was left free. On recovery from the anesthesia the patient was unable to void, but this was considered a sequel of the anesthesia. Three days after application of the cast, loss of power developed in both feet; he was unable to flex the toes. A slight edema of the left ankle (not included in the cast) developed.



Fig. 6.—Remains of cartilage cells. There are no evidences of inflammation.

Two days later (five days after the cast had been applied), he could not move his left leg (the right was in the cast) and there was incontinence of feces. On the following day, the cast was removed.

A neurologist who was called in consultation noted the following: 1. There was loss of deep and superficial sensation from the toes to the hips and loss of sensation around the anus. 2. The patient was unable to make any movements of either foot or leg below the knee. He could flex and extend the leg at the hip. This was some improvement, for two days earlier he was reported to be unable to make any movement of the leg. Paralysis was of the flaccid type. 3. Examination of the reflexes showed the ankle and right knee reflexes absent, the left knee reflex was diminished, and the abdominal and cremasteric reflexes were normal. 4. There was loss of vesical and rectal control. 5. Tenderness persisted over the third and fourth lumbar vertebrae. A lumbar puncture was done; the fluid was clear and colorless and registered 10 mm. of pressure with the mercurial manometer; jugular compression (Queckenstedt test) caused the pressure to rise instantly

to 30 mm., and on release of jugular pressure, the fluid promptly fell to the former level. The cell count was normal and there was no increase of globulin.

The patient was referred to me twelve weeks after the strain in the back and three weeks after the sciatic nerves had been stretched and the cast applied. The physical and neurologic observations were essentially the same as those just reported: 1. Sensation of every form was absent below the third lumbar segment but it was normal above this segmental level. 2. Flexion, adduction and extension of the leg at the hips were possible but decidedly weak while abduction was absent; there was no movement at the knee, ankle and toes. 3. All reflexes were abolished at and below the knee. 4. There was complete loss of vesical and rectal control. Lumbar puncture showed definite xanthochromia, the fluid having a greenish-yellow tint. The cell count was 10. The Queckenstedt test was negative, the column of fluid rising and falling with application and release of jugular compression. Iodized oil was injected; it descended only the distance of half a vertebra, lodging at the level of the fourth lumbar vertebra (fig. 2).

The only abnormality that could be detected in the roentgenograms (anteroposterior view only) was a supernumerary lumbar vertebra. The intervertebral disks appeared normal in size and shape.

Preoperative Impression.—That a tumor completely blocking the spinal canal was present at the level of the third lumbar vertebra seemed certain. That there was a definite relationship to the "stretching" of the sciatic nerves because of the sensory, motor and sphincter loss that occurred promptly thereafter could hardly be questioned. But it was necessary to admit that there was a preexisting lesion which had caused the severe pain in the back and down the legs. Though a metastatic lesion of the vertebra was suspected, no destruction of bone could be seen in the roentgenogram and no primary carcinoma could be found, though carefully sought. The true nature of the lesion was not suspected.

Operation.—Laminae of the fourth and fifth lumbar vertebrae (corresponding to the normal third and fourth) were removed under rectal ether anesthesia. Before the dura was opened, one could feel a hard mass about 1.5 cm. long, but when it was opened no tumor was visible. The roots of the cauda equina covered the exposed field. However, a sharply defined hillock of the cauda equina pushed backward, and under it one could still feel tumor of bony hardness. The roots of the cauda equina were definitely reddened and swollen. The cauda equina was retracted from the right side with a blunt dissector and a well circumscribed bulging extradural mass was at once visible; it crossed the midline posteriorly but was more on the right than the left. The mass was white, being covered with intact dura. When pressed firmly with the end of the forceps it seemed to fluctuate; at least it was soft in the center where it gave evidence of pointing. At once the picture of case 1 was recalled to mind for the gross appearance of the swelling was the same in both cases. The dura was slit longitudinally for a distance of about 1 cm. It was entirely avascular. A piece of loose cartilage projecting into the dural opening was picked up with the forceps and easily delivered (fig. 7). It was entirely unattached and no force was required to withdraw it. A few drops of fluid escaped with the floating cartilage. Further exploration of the cavity was not attempted. The borders of the cartilage were irregular; there was no sign of infection, no redness of the cartilage and no redness of the dura which covered the tumor. No fragments of bone were found attached to the cartilage. The cut edges of the dura sank back into the cavity from which the cartilage was removed. The knoll of the cauda equina entirely disappeared. The alinement of the vertebrae was normal.

Microscopic Report.—Exactly the same microscopic picture presented as in the preceding case. A few scattered cuts of cartilage were present, though in varying degrees of preservation. There was no cellular reaction indicative of an inflammation.

Subsequent Note.—The patient's recovery from the operation was uneventful. Urinary control returned ten days, and rectal control one month, after operation. Some sensation had returned within a month. He was beginning to walk four months after operation. Doubt of eventual complete recovery of motor function as in case 1 can scarcely be entertained, for the nerves are intact and apparently uninjured.

ANALYSIS OF CASES

In each case a large fragment of the intervertebral cartilage had become detached and was acting as a sequestrum. The reaction to the "foreign body" caused a swelling which bulged dorsally into the spinal canal (fig. 8). Pressure on the roots of the cauda equina then produced paralysis of all function below the nerve level of the tumor and through edema some function was lost for distance above the tumor.



Fig. 7.—Loose cartilage removed from patient in case 2.

The detached cartilage is almost certainly the result of trauma, but a relatively trivial trauma. In the first case no history of trauma was given voluntarily; it was elicited only after trauma was suspected. The trauma in the second case was almost surely the slight wrench caused by pushing an automobile. Several attacks of pain identical in both character and location were again induced by slight trauma before the advent of paralysis, and the location of the pain remained the same after the paralysis developed. The severe trauma incident to "stretching the sciatic nerves" and to placing the body in the cast with the lumbar region flexed undoubtedly caused the lesion to fulminate and promptly to reach the stage of tumor formation some time in advance of the normal course of events.

The preoperative diagnosis of a lesion in the vertebra could hardly be questioned in either case, because the slightest movement of the lower part of the spine always brought on or intensified the pain. Moreover, the tense spasm of the erector spinae muscles and the sharply

localized severe tenderness of the spinous process offered supporting evidence of the strongest kind. In these respects the lesion is hardly different from carcinoma of the vertebra. In either condition, only the recumbent posture could long be tolerated.

In both patients, the pain radiated down the back of both legs but usually down one more than the other. The side most involved proved to be the side of the greater bulge of the tumor. These facts lead one to wonder whether bilateral sciatic pains do not in most instances indicate a lesion affecting the spinal cord or cauda equina, more frequently

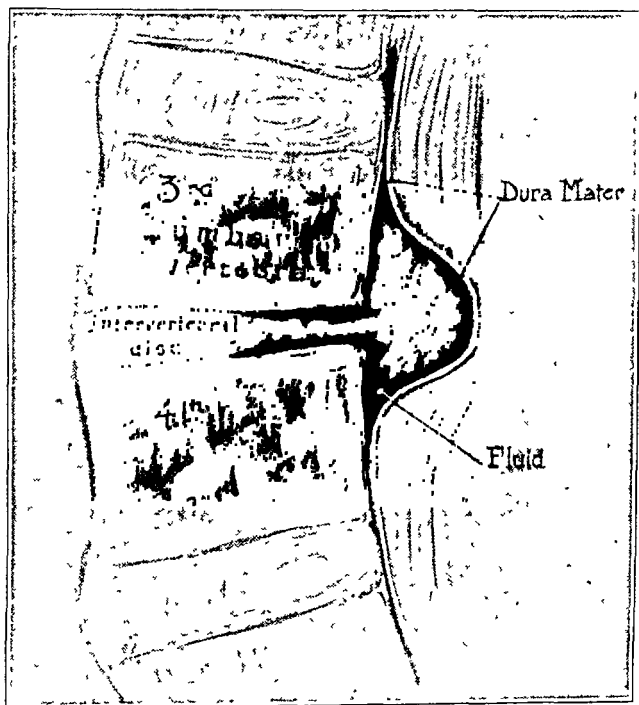


Fig. 8.—Sketch to show conception of position and manner of formation of loose cartilage projecting into the spinal canal and compressing the cauda equina.

the latter. These cases at least offer pathologic evidence of a definite lesion inducing symptoms of so-called sciatica with its all too meager pathology.

That the floating cartilage in each of these cases was in the lumbar region is doubtless significant. The maximum effects of shocks and of torsion of the body are transferred to the lumbar spine. As protection against shocks, the intervertebral disks attain their greatest size in the lumbar region. That the lesion occurs about the middle of the lumbar spine is probably also because of an additional point of least

resistance, for here the maximum part of the anterior lumbar curve is attained. Certainly movable vertebrae on a curve offer the maximum opportunity for localized effects of trauma.

That the lesion occurs on the posterior instead of on the anterior aspect of the lumbar vertebra is probably also significant. The normal anterior curvature of the lumbar spine would be expected to throw greater localized effects of trauma on the posterior side of the disk. In other words, the cartilage should be more readily pinched posteriorly than anteriorly. Then, too, the relatively thin and incomplete posterior ligaments of the lumbar spine should more readily permit protrusion of a tumor in the intervertebral disk than the stronger and complete anterior ligament. Whether a loose cartilage could push through the strong and firmly attached anterior ligament can only be conjectured. There is as yet no evidence that a loose cartilage forms only in the posterior part of the disk though it may well be possible. From the size of the extended cartilage as seen at operation, it is hardly possible that more than a third or at most a half of the anteroposterior diameter of the disk can be involved.

Finally, in both instances the tumor presented not in the midline but to one side. Doubtless the explanation for this fact is that the posterior common ligament is defective laterally along the lumbar spine. Since the lesion is of traumatic origin it is probably not without significance that both of these patients are men. It is also not improbable that the additional lumbar vertebra in one patient may have had some part in making the lumbar spine susceptible to injury.

Emphasis has been placed on the seemingly trivial injuries that cause the cartilaginous sequestrum formation. It is not improbable that the repetition of minor traumas may, at times, at least, be an important factor. The history of the repeated attacks in case 2 suggests this possibility. There must be many instances in which the intervertebral cartilage sustains the degree and character of injury experienced in these two cases, and yet subsequently heals instead of going on to sequestration. It is difficult to believe that the complete detachment of the cartilaginous fragment does not require considerable time, and that with proper rest and fixation of the spine this outcome may be avoided. A remarkable contrast in the disposition of fragments of intervertebral cartilage is presented by severe fracture dislocations of the spine. There the cartilage is badly torn and frequently fragmented, but in the process of healing it is organized with bone and fibrous tissue into a solid mass.

The x-ray has disclosed nothing in either of these cases. After the character of the lesion was known, the roentgenograms were again inspected, with negative results. However, only anteroposterior views were taken before operation, and positive signs would hardly be expected from this view. However, shortly after operation on the

second patient, lateral stereoscopic views of the affected part of the spine were taken, and not the slightest defect could be seen. The absence of bone in the sequestrum might well preclude the delineation of the tumor.

DIAGNOSIS

It is not difficult to arrive at the diagnosis of a tumor of the cauda equina because of the progressive paralysis—sensory, motor and sphincter—and loss of reflexes. The rapid progression of these signs and the severe pain in the back, the rigid lumbar spine due to spasm of the erector spinae muscles and the marked tenderness over the spinus processes and laminae of the lumbar vertebrae are such as to make metastatic carcinoma of the body of the vertebra the most likely diagnosis. The absence of roentgenologic changes in the body of the vertebra would appear to carry much importance in the differential diagnosis between this lesion and metastatic carcinoma or sarcoma of the body of the vertebra. The malignant lesions are almost the only ones that offer difficulties in differential diagnosis.

Aside from the negative roentgen changes in the body of a vertebra, there seems to be no absolute differential objective evidence. Even the clinical and microscopic examinations of the cerebrospinal fluid may show no differences, for both lesions are extradural. Each may give a mild degree of xanthochromia and globulin increase. Both give a negative reaction to the Queckenstedt test if the block is caudal to the point of entry of the needle, and both show a complete block at the upper level of the tumor when iodized oil is injected.

In the differential diagnosis two considerations are all-important: (1) to make the clinical diagnosis of carcinoma only on absolute evidence, i. e., microscopic or roentgenologic, and (2) to accept the operative diagnosis of a malignant condition only on positive evidence. My willingness to accept suggestive evidence of malignancy nearly deprived the first patient of the opportunity of having the lesion explored. In fact, had he not been eager to grasp the faint hope which an operation offered, the lesion would not have been disclosed. Even at operation the bulging mass from the body of the vertebra was at first considered so surely malignant that there seemed little reason to open the tumor.

The order of return of the various functions is most interesting. In both cases the vesical control returned completely in about ten days. Rectal control returned in about one month in each instance. Sensation gradually returned in about a month, but motor power made no improvement whatever until from seven to eight weeks after the operation in the first case, and at the end of the second month the motor power had not yet returned in the second patient. In the first case the motor improvement came slowly and continued for several months.

RESEMBLANCE OF THIS LESION TO OSTEOCHONDritis DISSECANS
OR TRAUMATIC JOINT-MICE

Superficially at least, the loose vertebral cartilage appears to resemble the loose cartilage of the knee, elbow and ankle joint following osteochondritis dissecans described by König in 1888. They differ in that fragments of bone were not attached to the cartilage in either of my cases. The environment too is greatly different in that there is no cavity—even potential—as in the knee and elbow joints. More common in the knee joint than elsewhere, this condition has come to be recognized as a clinical entity, but the dividing line between osteochondritis dissecans and other joint-mice appears to be none too sharp. The distinction is usually made that in osteochondritis dissecans the loose bodies occur singly or at most in pairs, and that there is no evidence of inflammatory joint involvement elsewhere. König¹ could find no evidence of traumatic or constitutional origin and for that reason considered them to represent a distinct pathologic process. Barth² thought they were purely of traumatic origin. Ludloff, who first diagnosed them by roentgenograms and treated them surgically, thought that they were due to occlusions of end-arteries. Other authors (Freiberg and Wooley,³ Ridlon,⁴ Codman,⁵ Weil,⁶ Anglin⁷ and Troell⁸) have come to no more definite conclusion. Büdinger⁹ (1907), Axhausen¹⁰ (1914), Kappis¹¹ (1920) and Brackett and Hall¹² (1917) were more positive of their purely traumatic origin. They also called attention

1. König: Ueber freie Körper in den Gelenken, Deutsche Ztschr. f. Chir. **27**:90, 1888.

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3. Freiberg and Wooley: Osteochondritis Dissecans, Am. J. Orthop. Surg. **8**:477, 1910.

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5. Codman, E. A.: Formation of Loose Cartilages in the Knee Joint, Boston M. & S. J. **149**:427, 1903.

6. Weil, S.: Ueber doppelseitige symmetrische Osteochondritis dissecans, Beitr. z. klin. Chir. **78**:403, 1912; Ztschr. f. Chir. u. Mech. Orth., July, 1912.

7. Anglin, R. H.: Loose Bodies in the Knee, with Special Reference to Their Etiology and Growth, Brit. J. Surg. **1**:650 (April) 1914.

8. Troell, A.: The Origin of Free Bodies in the Knee with Special Reference to Osteochondritis Dissecans, Arch. f. klin. Chir. **105**:399, 1914.

9. Büdinger: Ueber traumatische Knorpelrisse im Kniegelenk, Deutsches Ztschr. f. Chir. **92**:510, 1907.

10. Axhausen: Die Entstehung der freien Gelenk-Körper und ihre Beziehungen zur Arthritis deformans, Arch. f. klin. Chir. **104**:581, 1914.

11. Kappis: Osteochondritis dissecans und traumatische Gelenkmäuse, Deutsche Ztschr. f. Chir. **157**:187, 1920.

12. Brackett, E. G., and Hall, C. L.: Osteochondritis Dissecans, Am. J. Orthop. Surg. **15**:79, 1917.

to the fact that the injury may be slight and repeated. The present trend of opinion seems to be that the term *osteocondritis dissecans* is a misnomer (for there is no evidence of inflammatory character), and that it is better to classify these loose bodies under *traumatic joint-mice*.

SUMMARY

1. Following slight (or repeated) trauma a fragment of an intervertebral disk may become detached, and eventually bulge into the spinal canal as a tumor. The "tumor" is composed of the cartilage and fluid formed by reaction to the foreign body.

2. Two instances of this lesion are reported, both being disclosed at operation. Both are in the midlumbar region, and both occurred in men during the latter half of life.

3. The trauma at onset is relatively trivial and perhaps repeated. The lesion is probably similar to *osteocondritis dissecans* or *traumatic joint-mice* of the elbow and knee joint.

4. The early symptoms are those of localized vertebral pain plus bilateral sciatica—one side being affected more than the other. Later, the symptoms are rapidly increasing paralysis, sensory and motor paralysis and loss of urinary and vesical control and of reflexes—all due to compression of the cauda equina.

5. The signs and symptoms suggest carcinoma of the vertebra. This preoperative diagnosis was made in both cases.

6. This lesion offers a pathologic basis for cases of "so-called sciatica," especially bilateral sciatica.

7. The lesion is cured by operative removal of the cartilage.

RENAL COUNTERBALANCE *

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CLEVELAND

The theory of renal counterbalance was introduced by Hinman¹ in 1922. Before this article appeared, little, if anything, had been written concerning the possibility of renal atrophy of disuse, and according to Hinman this type of renal atrophy was a new conception, even though a similar process had long been recognized in other organs, such as muscle and bone. It is remarkable that a conclusion had not been crystallized concerning atrophy of disuse when applied to the kidney. Indeed, the subject seems to have been unnoticed until Hinman applied it as the basis for his theory of renal counterbalance.

According to this theory, a kidney, after sustaining a temporary injury, as, for example, a temporary period of ureteral obstruction causing hydronephrosis, will go on to complete or almost complete atrophy if allowed to function in competition with its hypertrophic mate. Thus, if the ureter of a kidney is obstructed for two or three weeks, this kidney becomes hydronephrotic and its mate undergoes hypertrophy. If at the end of this time the obstruction to the ureter is relieved, the hydronephrotic kidney supposedly will be placed at a distinct disadvantage. According to the theory of renal counterbalance, the kidneys enter into functional competition and the weaker kidney eventually goes on to complete or almost complete atrophy. In the words of Hinman:

"The healthier side will gradually undergo a compensatory hypertrophy which may be so capable of counterbalance as to render the work of its weak assistant unnecessary, disuse atrophy of which will progressively occur. The reapportionment of functional activity after the alteration occurs by a competitive type of anatomic compensation."

He also stated:

"An animal cannot live after opposite nephrectomy, with a repair hydronephrosis of longer than from two to three weeks. Any repair hydronephrosis, even of

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1. Hinman, F.: Renal Counterbalance: An Experimental and Clinical Study with Reference to the Significance of Disuse Atrophy, *Tr. Am. Ass. Genito-Urin. Surg.* 15:241, 1922; Renal Counterbalance, *Arch. Surg.* 12:1105 (June) 1926.

two weeks, will usually eventuate in complete atrophy if the opposite kidney remains healthy and undisturbed. . . ."

The experiments quoted by Hinman on which this theory is based, although numerous and variegated, are somewhat inconclusive. The following two experiments are taken from Hinman's monograph and seem to have the most direct bearing on the subject. The author stated that he has carried out similar experiments, but unfortunately they were not completely reported in his publication.

"Experiment 5.—Late atrophy of hydronephrotic repair; ureteral obstruction of twenty-one days; repair period of 249 days.

"Dog 5, weighing 20 pounds (9 Kg.).

"There was a complete obstruction of the left ureter for twenty-one days. After a ureterocystoneostomy, and a drainage period of 249 days, the urine was free from bacteria and pus. The dog was killed, under ether, with preliminary functional study. The appearance time of phenolsulphonphthalein was four minutes for the right kidney, and eight minutes for the left. In the first fifteen minutes, 25 per cent of the dye was excreted by the right kidney, and 5 per cent by the left; in the second fifteen minutes, 20 per cent by the right kidney and 2.5 per cent by the left, the total excretion for the first half-hour being 45 per cent for the right kidney and 7.5 per cent for the left. At necropsy, the left kidney weighed 15 Gm.; the right, 48 Gm. The ureter was freely patent. There was no pelvic dilatation on section and no evidence of infection. [An illustration] shows that the left kidney was reduced to one third its size, and that, even in the gross, cortical atrophy was quite marked."

"Experiment 8.—Thirty days left hydronephrosis; left ureterocystoneostomy; seven days later, partial obstruction of right ureter. Killed in 390 days.

"Dog 8, a male shepherd, weighing 42 pounds (19.1 Kg.).

"Nov. 1, 1920, ligation of left ureter.

"Blood urea nitrogen, 18 mg. per hundred cubic centimeters; nonprotein nitrogen, 34 mg. per hundred cubic centimeters; phenolsulphonphthalein, 70 per cent in two hours. . . .

"December 2, left ureterocystoneostomy.

"December 9, partial ligation of right ureter. Under ether anesthesia and surgical asepsis, the abdomen was opened in the midline just below the umbilicus.

" . . . The right ureter was identified in its bed as low down as possible without disturbing the recent operative area behind the bladder. A short length of ureter was freed in an area about 3 cm. from its point of entry into the bladder, and a rubber band 2 mm. wide was placed around it and stretched. The ends of the band thus stretched were tied with silk so as to form a moderate constriction of the ureter. . . . The animal recovered slowly from the operation. . . . A month after operation, he seemed quite normal and ate normal amounts.

"Nov. 29, 1921, . . . urea nitrogen, 26 mg. per hundred cubic centimeters; nonprotein nitrogen, 49 mg. per hundred cubic centimeters, and creatinine, 1.93 mg. per hundred cubic centimeters.

"Jan. 4, 1922, killed. Necropsy: The dog was in excellent condition; the weight was 42.5 pounds (19.3 Kg.). . . . The animal had been passing well formed stools and clear urine. Phenolsulphonphthalein, the first hour, was 53 per cent;

the second hour, 20 per cent. Blood urea nitrogen was 21 mg. per hundred cubic centimeters; nonprotein nitrogen, 41 mg. per hundred cubic centimeters. The dog was killed with ether.

" . . . The abdominal organs, except for the genito-urinary tract, presented no lesions whatever. The heart was not enlarged and showed no pathologic alterations. The lungs were clear. A sample of urine from the right ureter was clear and showed a considerable amount of pigment. The urine from the left ureter was cloudy. It showed an equal amount of pigment. . . .

"The left kidney was normal in shape and slightly enlarged. It collapsed readily at the hilum with pressure, showing a slight degree of hydronephrosis. The ureter of the kidney was very large, being 1 cm. in diameter. It was not tortuous. Its opening lay in the midline of the bladder posteriorly and was fully patent. . . . The right kidney was very large and had a very thin wall. There was a crescentic nodule of parenchyma at its upper pole $1\frac{1}{2}$ cm. thick and 7 cm. long. In all other areas, the wall was of paper thinness. The ureter was slightly larger than that of the opposite side. It was 1.3 cm. in diameter. It was much thinner than the left ureter and very tortuous. Near the bladder, it presented an obstructed area, at which point the rubber band, placed Dec. 9, 1920, was localized. Beyond this, it was of normal diameter. The right ureterovesical orifice through which this ureter opened was normal in all respects. . . . Gentle pressure on the hydronephrotic sac caused a flow of fluid through this ureteral orifice. The wall of the bladder was normal in appearance. . . . The respective sizes and weights of the two kidneys were as follows:

	Length (Pole to Pole)	Width (Side to Side)	Depth (Hilum to Greater Curve)	Weight	Pelvic Capacity
Left kidney....	6.95 cm.	2.5 cm.	3.0 cm.	47 gm.	5 cc.
Right kidney...	16.00 cm.	8.0 cm.	7.5 cm.	52 gm. (empty)	400 cc.

"The nitrogen content of the urine from the left kidney was: urea nitrogen 0.0045 Gm. in 1 cc.; nonprotein nitrogen, 0.0065 Gm. in 1 cc. The nitrogen content of the urine from the right kidney was: urea nitrogen, 0.0039 Gm. in 1 cc.; nonprotein nitrogen, 0.0068 Gm. in 1 cc."

In the first of the foregoing experiments, a kidney injured by a complete ureteral obstruction lasting twenty-one days has in a period of repair of two hundred and forty-nine days become an organ weighing 15 Gm., which is about one-third the weight of its hypertrophic mate. Although the excretion of phenolsulphonphthalein was only 7.5 per cent in one-half hour, still, the experiment can hardly be considered as one in which the injured kidney has gone on to complete atrophy. Whether this kidney would have become completely atrophied after a longer period of competition, it is impossible to say. Our experiments do not indicate that this would have occurred. The second experiment shows that a markedly damaged hydronephrotic kidney possesses a remarkable power to undergo repair and hypertrophy if the functional demand is placed on it.

Should the theory of renal counterbalance become established, its clinical application would be of far-reaching importance. It would play a rôle in many types of renal surgery, for if the injury to one kidney

were continued over a sufficiently long period of time to allow the opposite kidney to become fully hypertrophied, the injured kidney would eventually go on to complete atrophy even though the injurious agent were removed. It would be useless, therefore, to carry out plastic operation on a hydronephrotic kidney if its mate had become fully hypertrophied. The plastic operation would have to be supplanted by a removal of the hydronephrotic kidney, since any operation for the relief of an obstruction would be useless so far as restoration of function in that kidney would be concerned. The theory would find application also in cases of unilateral stone in which there was destruction of parenchyma in the involved kidney and accompanying hypertrophy in its mate. The operation of pyelotomy or nephrotomy would be supplanted here by nephrectomy. Also in the treatment of bilateral nephrolithiasis the period of time between the operations for the removal of the stones from each kidney should not be long enough to allow one kidney to undergo hypertrophy.

EXPERIMENTAL TECHNIC

The experiments reported in this paper were conducted on healthy dogs and were of three types. A kidney (in our experiments always the right) was damaged by producing a complete obstruction of its ureter. The obstruction was temporary and its duration varied from twelve to nineteen days. In one group of experiments the animals were killed at the end of the period of obstruction so that the changes in the obstructed and nonobstructed kidneys could be studied. In all the other experiments, the right ureter was implanted into the bladder after the temporary period of obstruction. In one group of these experiments the hypertrophied mate was removed several days after the obstruction was relieved, while in another group the hypertrophied kidney was allowed to remain undisturbed.

In all the experiments, observations of the gross and of the histologic changes in the kidneys were made. Only those experiments are reported in which there was no evidence of renal infection or in which there was simply a mild degree of pyelonephritis. In practically all the experiments, preoperative and postoperative studies of the blood urea were made.

Each operation was carried out under strictly aseptic precautions. Open ether anesthesia was used, preceded by a subcutaneous injection of 0.015 Gm. of morphine. The operative procedures are described in detail in the following paragraphs, and to avoid repetition will be referred to in the protocols only by name.

Ligation of Ureter.—The abdomen was opened through a suprapubic midline incision about 4 cm. long. The bladder was brought into the wound, and the right ureter was isolated close to the bladder. Here the ureter was doubly ligated with silk and cut between ligatures. The structures were replaced in the abdominal cavity, and the wound was closed in layers with silk.

Implantation of the Ureter into the Bladder.—The hydronephrosis was relieved in each experiment by implanting the ureter into the bladder. The abdomen was opened through a right rectus incision. The bladder was elevated into the wound, and the proximal end of the ureter was isolated. It was dissected free for about 2 cm.; its ligated end was excised, and, after allowing the urine to drain off, the end of the ureter was split longitudinally for about 0.5 cm. A suture of fine

catgut was placed in each end of the split ureter. An incision about 6 mm. long was made through the posterior wall of the bladder, and through this opening the ends of the ureter were inserted. The split ends of the ureter were then separated in opposite directions and the sutures of catgut were completed by passing each end through the wall of the bladder and were tied. The incision in the wall of the bladder was closed around the ureter and one or two sutures were passed between the bladder and the adventitia of the ureter. Care was taken to avoid obstruction at the new ureteral orifice. The structures were replaced in the abdominal cavity and the wound was closed in layers with silk.

Nephrectomy.—The left kidney was removed through either a left rectus or a left lumbar incision. The kidney was freed and delivered; the ureter and renal vessels were doubly ligated and cut between ligatures. The wound was approximated in layers with silk.

EFFECTS ON KIDNEYS OF THIRTEEN TO SIXTEEN DAY PERIODS OF UNILATERAL COMPLETE URETERAL OBSTRUCTION

PROTOCOL 1.—In dog A 51, a male mongrel, weighing 17.9 Kg., hydronephrosis was produced for sixteen days.

Sept. 23, 1927: The right ureter was ligated.

October 9: The dog was killed to obtain specimens of the kidneys after sixteen days of complete ureteral obstruction. The results of the general necropsy were negative. The right kidney showed a marked degree of hydronephrosis and dilatation of the ureter. The left kidney showed compensatory hypertrophy. The weights and measurements of the kidneys were:

	Right	Left
Weight	59.0 Gm.	76.8 Gm.
Length	7.5 cm.	7.5 cm.
Transverse diameter.....	4.9 cm.	5.2 cm.
Anteroposterior diameter.....	2.8 cm.	3.6 cm.
Capacity of pelvis.....	43.0 cc.	3.5 cc.
Cortex	7.0 mm.	10.0 mm.

The appearance of the kidneys is shown in figure 1. The pyelogram of the right kidney (fig. 2) showed a marked dilatation of the pelvis, calices and ureter, and a definite thinning of the parenchyma. The pyelogram of the left kidney was normal.

Histologic Observations.—In the left kidney, there was a diffuse hyperemia, particularly of the glomeruli which appeared very large, with occasional collections of serum precipitate in the capsular spaces.

In the right kidney, the glomeruli appeared concentrated in comparison to their distribution in the left kidney. The glomerular tufts showed no pathologic change, but occasionally there were small amounts of serum precipitate in the capsular spaces. There were patchy areas of tubular dilatation and widespread tubular atrophy. The tubular dilatation was most marked in the superficial zone of the cortex which was also the seat of interstitial fibrosis.

PROTOCOL 2.—In dog A 52, a white female mongrel, weighing 12.4 Kg., hydronephrosis was produced for fourteen days.

Sept. 29, 1927: The right ureter was ligated.

October 13: The dog was killed to obtain specimens of the kidneys after fourteen days of complete ureteral obstruction. The results of the general

necropsy were negative. The right kidney was hydronephrotic, and its ureter was dilated. The left kidney showed compensatory hypertrophy. The weights and measurements of the kidneys were:

	Right	Left
Weight	55.4 Gm.	56.0 Gm.
Length	8.0 cm.	7.2 cm.
Transverse diameter.....	4.5 cm.	4.6 cm.
Anteroposterior diameter.....	3.2 cm.	2.8 cm.
Capacity of pelvis.....	20.0 cc.	...
Cortex	7.0 mm.	8.0 mm.

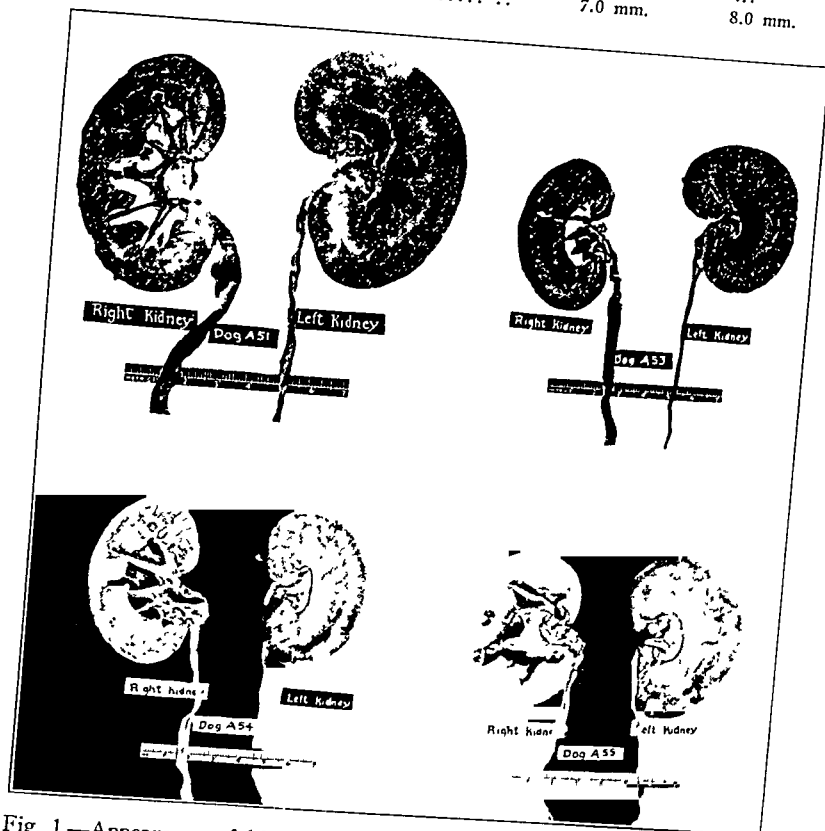


Fig. 1.—Appearance of kidneys after complete obstruction of the right ureter for sixteen, fourteen, thirteen and thirteen days, respectively, showing the marked damage (table 1).

The pyclogram of the right kidney (fig. 2) showed a moderate dilatation of the ureter and a marked dilatation of the pelvis and calices. The pyclogram of the left kidney was normal.

Histologic Observations.—The glomeruli in the left kidney were large, and occasional collections of serum precipitate were observed in the capsular spaces. The tubules showed no pathologic change. There was marked hyperemia of both cortex and medulla.

The glomeruli in the right kidney were uniformly small and in many of them there was partial or complete necrosis of the tufts (fig. 3). The necrotic portions

had a granular basophilic appearance with fragmentation and pyknosis of nuclei. In some instances, only a small fragment of the tuft was left intact and the capsular space contained a large amount of granular debris. There was widespread collapse and atrophy of tubules, which was particularly prominent in the superficial zone of the cortex. There was some slight diffuse increase of interstitial connective tissue.

PROTOCOL 3.—In dog A 53, a male mongrel, weighing 12.7 Kg., hydronephrosis was produced for fourteen days.

Sept. 29, 1927: The right ureter was ligated.

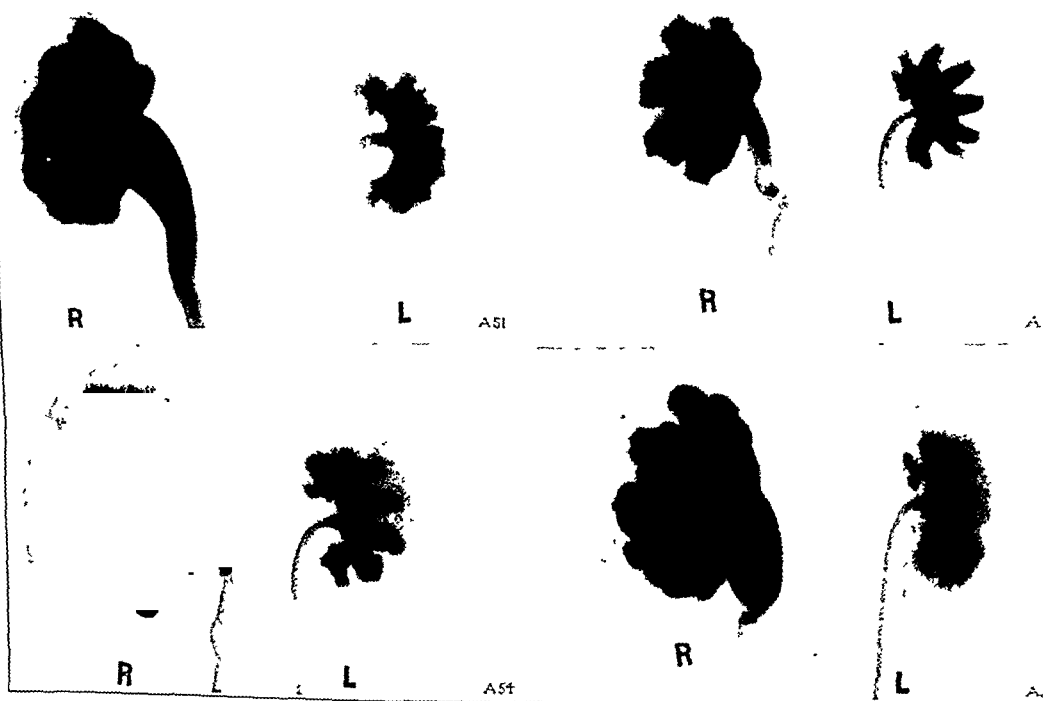


Fig. 2.—Pyclograms of kidneys after complete obstruction of the right ureter for sixteen, fourteen, thirteen and thirteen days, respectively.

October 13: The dog was killed to obtain specimens of the kidneys after a period of fourteen days of complete ureteral obstruction. The results of the general necropsy were essentially negative. The right kidney was distinctly hydronephrotic with dilatation of the ureter. Its urine showed no evidence of infection. The left kidney appeared to be hypertrophic. The weights and measurements of the kidneys were:

	Right	Left
Weight	31.4 Gm.	47.0 Gm.
Length	6.7 cm.	6.4 cm.
Transverse diameter.....	3.8 cm.	5.0 cm.
Anteroposterior diameter..	2.4 cm.	2.9 cm.
Cortex	4.0 mm.	7.0 mm.

The appearance of the kidneys is shown in figure 1.

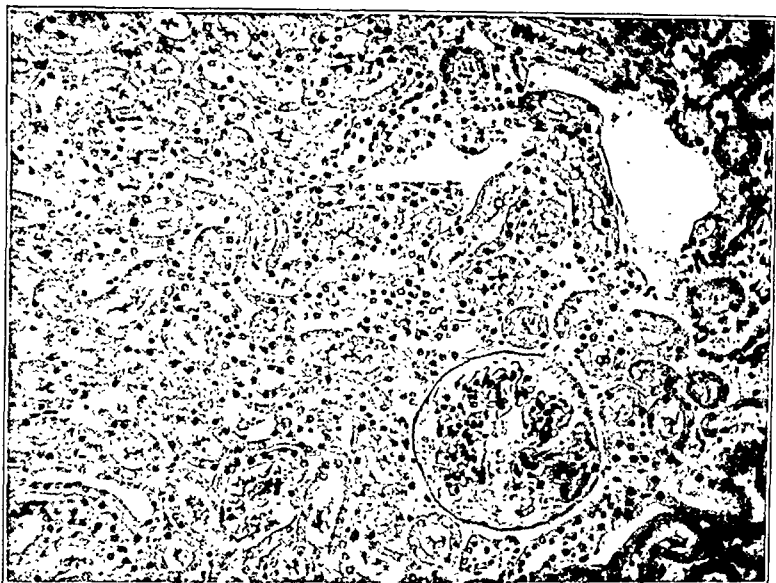


Fig. 3.—Cortex of right kidney of dog A 52, protocol 2, showing necrosis of a portion of a glomerular tuft; $\times 65$.

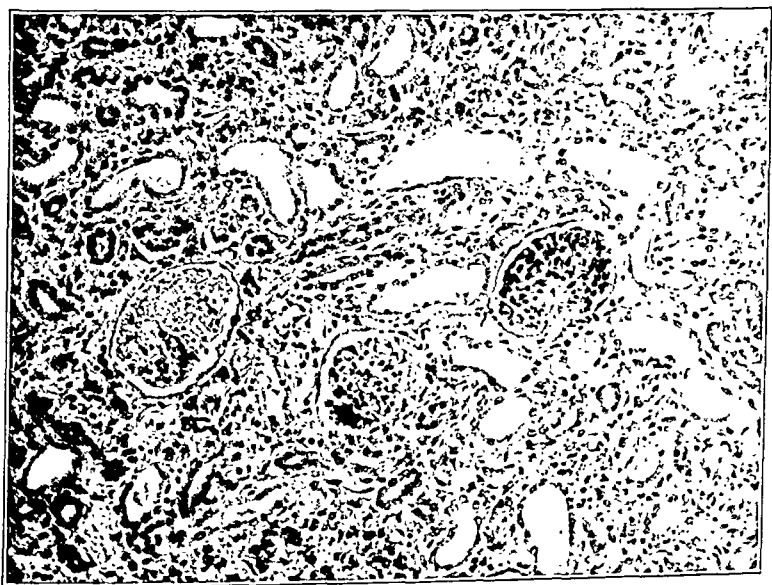


Fig. 4.—Cortex of right kidney of dog A 53, protocol 3, showing a partially necrotic glomerular tuft and many atrophic, collapsed tubules. There is a diffuse increase in interstitial fibrous connective tissue and dilatation of the loops of Henle; $\times 65$.

Histologic Observations.—The glomeruli in the left kidney appeared larger than normal, and the tufts were distended with red blood cells. Many glomeruli showed collections of serum precipitate in the capsular spaces. The tubules appeared normal except for swelling and granularity of the epithelium. The interstitial tissue was moderately edematous. Both cortex and medulla were hyperemic.

In comparison to the left kidney, there appeared to be a concentration of glomeruli in the right kidney, especially in the superficial zone of the cortex. Some of the glomeruli appeared normal, but a great many manifested varying degrees of degenerative changes ranging from pyknosis of a few nuclei to necrosis of the entire tuft (fig. 4). There was marked tubular atrophy, many of the tubules being represented only by a small solid group of epithelial cells surrounded by a basement membrane. Occasional dilated tubules were seen. There was diffuse increase of interstitial fibrous connective tissue which was most pronounced in the medulla and in the cortex corticis.

PROTOCOL 4.—In dog A 54, a young male hound, weighing 9.8 Kg., hydronephrosis was produced for thirteen days.

Sept. 30, 1927: The right ureter was ligated.

October 13: The dog was killed to obtain specimens of the kidneys after a period of thirteen days of complete ureteral obstruction. The results of the general necropsy were negative. The right kidney was large and hydronephrotic and the ureter was dilated. The urine from this kidney showed no evidence of infection. The left kidney appeared to be normal but somewhat hypertrophic. The weights and measurements of the kidneys were:

	Right	Left
Weight	48.5 Gm.	61.8 Gm.
Length	7.5 cm.	6.8 cm.
Transverse diameter.....	4.8 cm.	5.0 cm.
Anteroposterior diameter.....	2.0 cm.	2.7 cm.
Cortex	3.5 mm.	6.0 mm.
Capacity of pelvis.....	80.0 cc.	...

The appearance of the kidneys is shown in figure 1. The pyelogram of the right kidney (fig. 2) showed a very marked degree of hydronephrosis with a thin parenchyma. The pyelogram of the left kidney was normal.

Histologic Observations.—The glomeruli in the left kidney were large and the tufts hyperemic and usually completely filled the capsular spaces. The capsules occasionally contained a small amount of serum precipitate. There was moderate parenchymatous degeneration of the tubular epithelium. Both cortex and medulla were intensely hyperemic, and the tubules were widely separated by distended capillaries and edematous interstitial connective tissue.

The changes in the right kidney were essentially the same as those in the right kidney of dog A 53 (protocol 3), except that there was more widespread degeneration of glomeruli and many glomeruli with normal appearing tufts showed proliferation of capsular epithelium. The pyramids were the seat of pronounced tubular atrophy and fibrosis.

PROTOCOL 5.—In dog A 55, a young female hound, weighing 8.7 Kg., hydronephrosis was produced for thirteen days.

Sept. 30, 1927: The right ureter was ligated.

October 13: The dog was killed for specimens of the kidneys after a period of thirteen days of complete ureteral obstruction. The results of the general necropsy were negative. The right kidney was markedly hydronephrotic, and its ureter was dilated. The urine showed no evidence of infection. The left kidney

was darker and more congested than the right and appeared to be hypertrophic. The weights and measurements of the kidneys were:

	Right	Left
Weight	45.0 Gm	46.0 Gm
Length	8.2 cm	6.6 cm
Transverse diameter.	4.8 cm	3.4 cm.
Anteroposterior diameter.	2.4 cm	2.6 cm.
Cortex	5.0 mm	8.0 mm
Capacity of pelvis.	50.0 cc	.

The appearance of the kidneys is shown in figure 1. The pyelogram of the right kidney (fig. 2) showed a marked degree of hydronephrosis. The pyelogram of the left kidney was normal.

Histologic Observations.—Left Kidney: The glomeruli were large, and the tufts were plump and in most instances filled their capsules. Occasional glomeruli showed partial necrosis of the tuft, manifested by loss of nuclei with granular degeneration of the cytoplasm. There was a moderately severe parenchymatous degeneration of the tubular epithelium. The interstitial tissue was edematous and hyperemic.

TABLE 1—Data on Dogs Following Unilateral Complete Ureteral Obstruction

Protocol	Duration of Complete Obstruction of Right Ureter, Days	Weight of Kidneys, Gm		Percentage of Total Renal Mass	
		Right	Left	Right	Left
1 (Dog A 51)	16	59.0	76.8	43.4	56.6
2 (Dog A 52)...	14	55.4	58.0	49.7	50.3
3 (Dog A 53)...	14	31.4	47.0	40.0	60.0
4 (Dog A 54)...	13	48.5	61.8	43.9	56.1
5 (Dog A 55)...	13	45.0	46.0	49.5	50.5

In the right kidney, there was a concentration of glomeruli in the subcapsular zones of the cortex and many of them were partially or completely necrotic. The tubules were predominantly atrophic although a few distended loops were seen. Parenchymatous degeneration of tubular epithelium was present. In general, the sections appeared very similar to those from the right kidneys of dogs A 53 and A 54 (protocols 3 and 4).

These five experiments are recorded to show the effects on the kidneys of periods of from thirteen to sixteen days of unilateral complete ureteral obstruction. It can be seen from the descriptions and illustrations (figs. 1 and 2) that a fairly marked degree of hydronephrosis and renal damage was produced by the ureteral obstruction. The relatively slight differences in weight between the hydronephrotic right kidney and the hypertrophic left kidney are striking and especially interesting when compared with the relative weights of the kidneys of some of the other experiments.

A summary of the histologic changes observed in this group of experiments follows:

The undisturbed left kidneys of these animals were fairly uniform in their histologic appearances. Both cortex and medulla were intensely

hyperemic with considerable interstitial edema, particularly of the cortex. The glomeruli were large, and the hyperemic tufts tended to fill their capsular spaces. The presence of serum precipitate within the glomerular capsule was a common occurrence.

The obstructed right kidneys showed considerable variation in the extent of the pathologic changes. The earliest change was manifested in the tubules and interstitial tissue (fig. 4). Dilatation as well as atrophy and collapse of tubules, with interstitial edema, was seen in kidneys showing no glomerular damage. The extent of tubular atrophy varied but was most marked in those kidneys showing glomerular damage. The glomerular changes consisted of partial or complete necrosis of the tufts (figs. 3 and 4). The number of tufts damaged varied in different animals but in none of them did the damaged tufts outnumber those that appeared normal. The necrosis manifested itself by a basophilic, granular degeneration of the cytoplasm with pyknosis, fragmentation, and disappearance of nuclei. Occasional masses of granular cellular debris were present in the capsular spaces around necrotic tufts. In one animal there was moderate proliferation of the capsular epithelium. There was a diffuse increase in interstitial fibrous connective tissue, most pronounced in the medulla and in the subcapsular zone of the cortex. In the fibrosed outer zone of the cortex proper the glomeruli appeared especially numerous, and it was in these concentrated glomeruli that the most severe damage was manifest.

REPAIR OF HYDRONEPHROTIC KIDNEYS WITH REMOVAL OF HYPERTROPHIC MATE

Protocol 6.—In dog A 20, a female collie, weighing 14 Kg., hydronephrosis was produced for eleven days followed by a period of repair of eight hundred and twenty-eight days.

Jan. 9, 1925: The blood urea was 38 mg. per hundred cubic centimeters.

January 13: The blood urea was 23 mg. The right ureter was ligated

On January 15, the blood urea was 14.1 mg.; on January 22, 50.1 mg.

January 24: The right ureter was implanted into the bladder after a period of eleven days of complete ureteral obstruction.

January 26: The blood urea was 33 mg. Left nephrectomy was performed. The left kidney appeared to be grossly normal although it was somewhat hypertrophied. The weight and measurements were: weight, 34.5 Gm.; length, 6 cm.; transverse diameter, 3.8 cm.; anteroposterior diameter, 2.8 cm.; cortex, 7 mm.

February 3: The blood urea was 140.4 mg., but in spite of this the dog appeared to be in good general condition.

On February 9, the blood urea was 112.3 mg.; February 13, 102 mg.; February 26, 69 mg.; March 16, 40.2 mg.; March 25, 66.8 mg.; April 1, 53.5 mg.; April 10, 53.5 mg.; May 7, 62.5 mg.; June 25, 27 mg.; July 22, 43.2 mg. (condition excellent); September 24, 44 mg.; October 16, 37 mg.; November 13, 42 mg.; December 23, 80 mg.

Jan. 4, 1926: The dog gave birth to a litter of seven pups.

January 14: Her general condition was excellent. The blood urea was 68.5 mg.

On February 13, the blood urea was 44.5 mg.; March 17, 57.8 mg.; June 24, 68.4 mg.; August 17, 37 mg.

September 1: The dog gave birth to a litter of seven pups.

On October 13, the blood urea was 32 mg.; November 19, 53 mg.

December 23: The microscopic examination of the urine showed no pus cells, red blood cells or casts.

On Jan. 24, 1927, the blood urea was 54 mg.; March 4, 41 mg.; April 26, 36 mg.

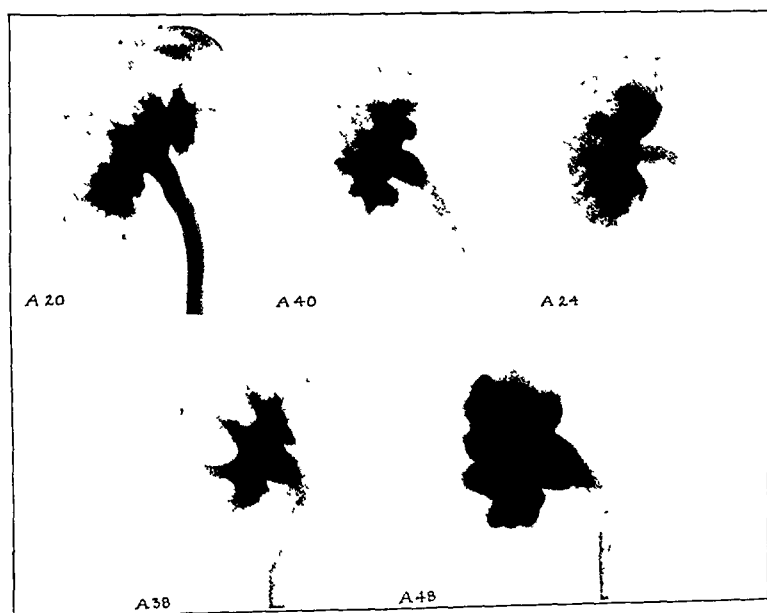


Fig. 5.—Pyelograms of the obstructed right kidneys of dogs A 20, A 40, A 24, A 38 and A 48, showing a tendency of the pelvis to return to normal shape and size.

May 2: For the past few days the dog appeared sick, and on this date she was found dead in the kennels.

Necropsy.—There were no external signs of violence. The heart was normal. The lungs showed some small patches of pneumonia. On opening the abdominal cavity, about 100 cc. of dark fluid was found. All the abdominal organs except the pancreas and kidneys were normal. The former showed definite gross and microscopic evidence of an acute pancreatitis. The left kidney had been removed at a previous operation. The right kidney appeared to be hypertrophic. Its ureter was slightly dilated at its upper portion for a distance of about 4 cm. but below this it was normal. The anastomosis of the ureter into the bladder was satisfactory and appeared to be perfectly patent. The bladder was normal. The weight and measurements of the right kidney were: weight, 582 Gm.; length, 7.5 cm.; transverse diameter, 5 cm.; anteroposterior diameter, 3 cm.; capacity of pelvis,

5.9 cc.; cortex, 4 mm. A pyelogram showed a slight degree of dilatation of the upper portion of the ureter and the pelvis, but was otherwise not remarkable except that a small amount of the sodium iodide had extravasated into the parenchyma in the region of the lower pole (fig. 5). The gross appearance of the kidneys is shown in figure 6.

Histologic Observations.—The glomeruli in the left kidney appeared large with plump, hyperemic tufts which filled their capsules completely. There was a moderate degree of parenchymatous degeneration of the tubular epithelium. Otherwise, there was no pathologic change.

The histologic examination of the right kidney was rendered somewhat unsatisfactory by the amount of postmortem change present. The glomeruli were very large and hypertrophic, with plump cellular tufts which filled their capsules. The usual difference in size between peripheral and central glomeruli was not present and those in the outer zone of the cortex were as large as those in the corticomedullary zone. A few thickened capsules were seen. There was a mild, patchy chronic pyelonephritis, and in the densely infiltrated radial scars the glomeruli were fibrosed and atrophic and the tubules filled with pus cells.

PROTOCOL 7.—In dog A 33, a white and brown female mongrel, weighing 7 Kg., hydronephrosis was produced for fifteen days, followed by a period of repair of five hundred and five days.

On May 18, 1925, the blood urea was 25.5 mg. per hundred cubic centimeters, and on May 25, 47 mg.

May 25: The right ureter was ligated.

On May 27, the blood urea was 49 mg.; on June 9, 33 mg.

June 9: The ureter was implanted into the bladder after a period of fifteen days of complete ureteral obstruction.

June 11: The blood urea was 25 mg. Left nephrectomy was performed. The left kidney appeared grossly normal. The weight and measurements were: weight, 38 Gm.; length, 5.1 cm.; transverse diameter, 3.6 cm.; anteroposterior diameter, 2.5 cm.; cortex, 6 mm.

On June 15, the blood urea was 174.4 mg., but the general condition of the dog seems good. On June 24, it was 80 mg.; on July 8, 76.9 mg.

July 30: The dog gave birth to a litter of five pups.

On September 24, the blood urea was 24 mg.; November 13, 52 mg.; Feb. 13, 1926, 87.7 mg.; March 17, 67.6 mg.; April 29, 65.3 mg.; June 3, 70.2 mg.; June 24, 67.6 mg.; August 16, 23 mg.; October 13, 37 mg.

October 27: The dog was killed in a fight.

Necropsy: The dog sustained extensive wounds of the thoracic wall and right lumbar region. Through the lumbar wound the right kidney had been somewhat lacerated. Aside from these wounds, the results of the necropsy were negative. The right kidney, aside from its lacerations, appeared to be normal. It was firm on palpation and the cut surface showed a normal medulla and cortex. The pelvis and ureter were not dilated. The implantation of the ureter into the bladder was satisfactory and appeared to be perfectly patent. The weight was 32 Gm., and the cortex measured 6 mm.

The gross appearance of the kidneys is shown in figure 6.

Histologic Observations.—In the left kidney, there was diffuse hyperemia and the glomerular tufts were plump, filling their capsules. The tubular epithelium was the seat of moderate parenchymatous degeneration.

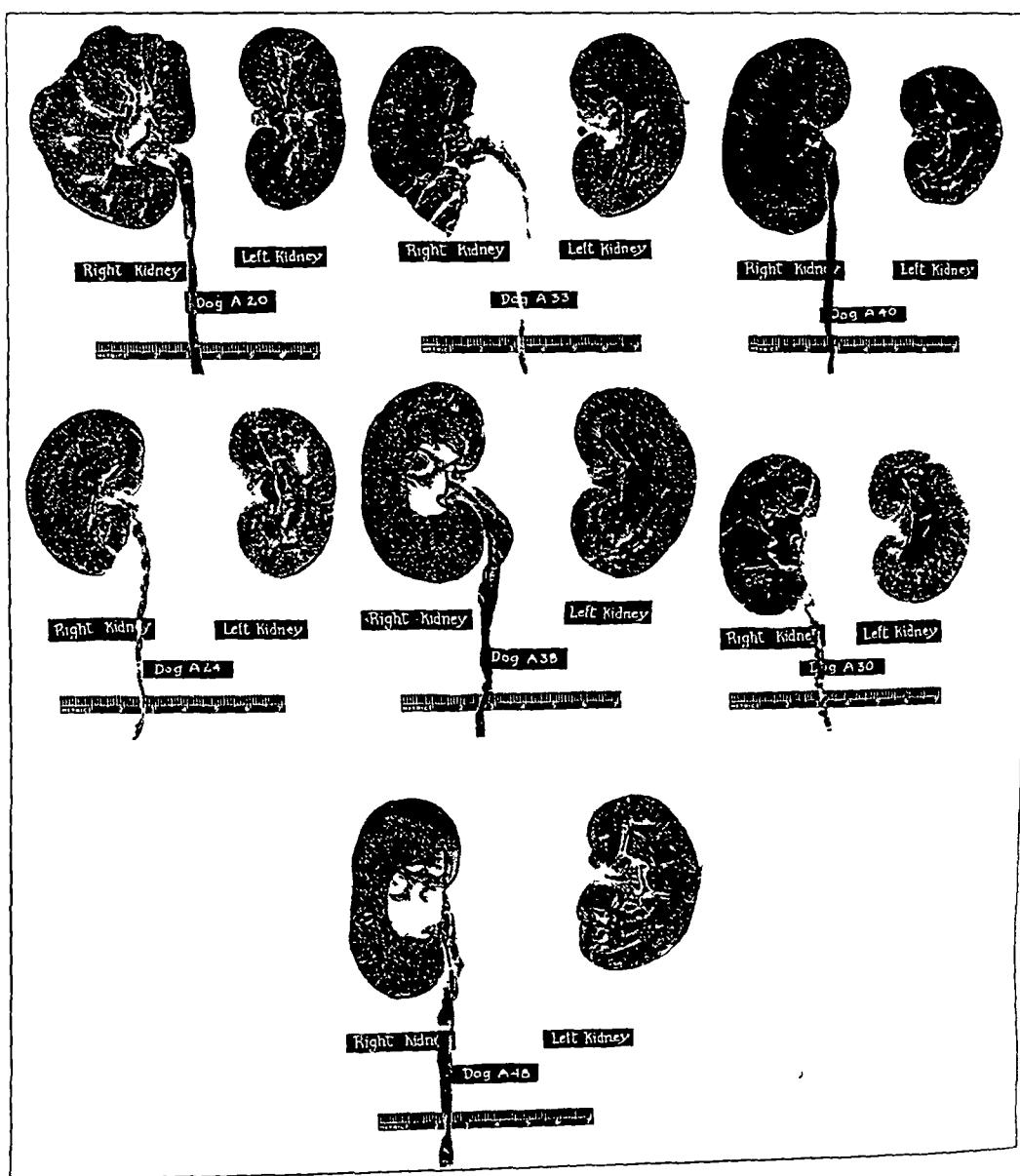


Fig. 6.—Appearance of kidneys of experiments of group II, showing the repair and hypertrophy which the hydronephrotic right kidney undergoes after removal of its mate (table 2).

In the right kidney, most of the glomeruli were large and hypertrophic, and there was a collection of serum precipitate within the capsules of many of them. Occasional small fibrosed glomeruli with thickened capsules were encountered. There was no evidence of interstitial fibrosis. The normal architecture was preserved.

PROTOCOL 8.—In dog A 40, a male mongrel, weighing 10.3 Kg., hydronephrosis was produced for fifteen days, followed by a period of repair of two hundred and ninety-three days.

On May 18, 1925, the blood urea was 25.5 mg. per hundred cubic centimeters.

May 25, 1925: The right ureter was ligated. On May 27, the blood urea was 51 mg.; on June 9, 34 mg.

June 9: The ureter was implanted into the bladder after fifteen days of complete ureteral obstruction.

June 11: The blood urea was 31.2 mg.

June 11: Left nephrectomy was performed. The left kidney appeared somewhat hypertrophied but otherwise normal. The weight and measurements were: weight, 36.7 Gm.; length, 6 cm.; transverse diameter, 3.8 cm.; anteroposterior diameter, 2.6 cm.; cortex, 5 mm.

On June 15, the blood urea was 144 mg., but the animal's general condition seems to be good. On June 24, it was 59 mg.; July 8, 54 mg. (weight, 9.3 Kg.); July 31, 59.1 mg.; August 13, 51 mg.; September 24, 48 mg.; October 16, 45 mg.; November 13, 43 mg.; December 23, 50 mg.; Jan. 14, 1926, 52 mg.; February 13, 29.5 mg.; March 17, 47 mg.

March 29: The dog was killed.

Necropsy.—The results of necropsy were negative except the changes found in the urinary tract. The right kidney appeared to be normal and somewhat hypertrophied. The right ureter was slightly dilated. The implantation of the ureter into the bladder was satisfactory and perfectly patent. The weight and measurements of the right kidney were: weight, 40.6 Gm.; length, 6.4 cm.; transverse diameter, 3.8 cm.; anteroposterior diameter, 2.5 cm.; cortex, 5 mm.; capacity of pelvis, 4 cc. A pyelogram appeared relatively normal except for the slight dilatation of the ureter and pelvis (fig. 5). The gross appearance of the kidneys is shown in figure 6.

Histologic Observations.—Except for the general glomerular hypertrophy and the presence of occasional fibrosed, atrophic glomeruli with thickened capsules in the right kidney there was no histologic difference in the two kidneys of this animal. There was no scarring or increase in interstitial fibrous connective tissue.

PROTOCOL 9.—In dog A 24, a brown and white, short haired, male mongrel, weighing 9 Kg., hydronephrosis was produced for twelve days followed by a period of repair of one hundred and fifty-five days.

On Jan. 22, 1925, the blood urea was 43 mg.; on January 27, 27 mg.

January 30: The right ureter was ligated.

On February 3, the blood urea was 32 mg.; on February 9, 44 mg.

February 11: The right ureter was implanted into the bladder after a period of twelve days of complete ureteral obstruction.

February 13: The blood urea was 43 mg.

February 13: Left nephrectomy was performed. The kidney appeared somewhat hypertrophied but otherwise normal. The weight and measurements were: weight, 30.9 Gm.; length, 6 cm.; transverse diameter, 3.7 cm.; anteroposterior diameter, 2.9 cm.; cortex, 6 mm.

On February 16, the blood urea was 85.1 mg.; February 26, 47 mg.; March 9, 24.9 mg.; March 25, 40.2 mg.; April 1, 40.2 mg.

April 10: The dog had been losing weight and had mange. On this date it weighed 6.5 Kg. The blood urea was 43.2 mg.

April 16: The dog's condition seemed better. The blood urea was 24 mg.

May 7: The blood urea was 46 mg.

June 25: The dog was in good condition. The blood urea was 33 mg.

July 14: The dog was killed.

Necropsy.—No abnormalities were found in any of the organs except those of the urinary tract. The right kidney was grossly normal except that it appeared somewhat hypertrophied. The implantation of the ureter into the bladder was satisfactory and perfectly patent. The right ureter and pelvis appeared to be normal. The weight and measurements of the kidney were: weight, 34.1 Gm.; length, 6.1 cm.; transverse diameter, 3.6 cm.; anteroposterior diameter, 2.6 cm.; cortex, 5 mm.; capacity of pelvis, 3.5 cc. A pyelogram showed no abnormalities (fig. 5). The appearance of the kidneys is shown in figure 6.

Histologic Observations.—In the left kidney, the glomeruli were plump and hyperemic, and occasional collections of serum precipitate were present in the capsular spaces.

In the right kidney, there was no evidence of interstitial fibrosis in the cortex. The glomeruli appeared normal except for serum precipitate in the glomerular spaces. The arcuate arteries showed a zone of peri-arterial fibrosis. There was a moderate diffuse increase of fibrous connective tissue in the pyramids.

Protocol 10.—In dog A 38, a black and white female mongrel, weighing 16 Kg., hydronephrosis was produced for sixteen days followed by a period of repair of seventy-nine days.

May 18, 1925: The blood urea was 43.3 mg. per hundred cubic centimeters.

May 20: The right ureter was ligated.

On May 25, the blood urea was 54.5 mg.; on June 3, 47 mg.

June 5: The right ureter was implanted into the bladder after a period of sixteen days of complete ureteral obstruction.

June 8: The blood urea was 43.2 mg.

June 8: Left nephrectomy was performed. The kidney appeared hypertrophied but was otherwise normal. The weight and measurements were: weight, 45.1 Gm.; length, 6.6 cm.; transverse diameter, 3.8 cm.; anteroposterior diameter, 2.7 cm.; cortex, 7 mm.

On June 15, the blood urea was 161 mg.; June 24, 76 mg.; July 8, 62.4 mg.

July 31: The animal's condition was poor. She appeared thin, weak and mangy. The blood urea was 108 mg.

August 13: The dog's general condition seemed much better. The blood urea was 122.1 mg.

August 23: The animal was found dead in the kennels.

Necropsy.—No definite cause of death was found. All the organs seemed normal. The weight and measurements of the right kidney were: weight, 44.5 Gm.; length, 6.2 cm.; transverse diameter, 3.8 cm.; anteroposterior diameter, 2.7 cm.; cortex, 4 mm. The anastomosis of the ureter into the bladder was perfectly patent. The ureter and pelvis were somewhat dilated. A pyelogram was made which, aside from some dilatation of the ureter and pelvis, was relatively normal (fig. 5). The gross appearance of the kidneys is shown in figure 6.

Histologic Observations.—The glomeruli of the left kidney were hyperemic, and many of them contained serum precipitate within the capsular spaces.

The glomeruli of the right kidney were larger than in the left kidney. There was a moderate amount of scarring in the pyramids; otherwise the two kidneys were histologically identical.

PROTOCOL 11.—In dog A 30, a brown and white male mongrel, weighing 6.9 Kg., hydronephrosis was produced for sixteen days followed by a period of repair of forty-two days.

May 18, 1925: The blood urea was 25 mg. per hundred cubic centimeters.

May 19: The right ureter was ligated.

On May 21, the blood urea was 26.7 mg.; May 25, 51 mg.; June 3, 56 mg.

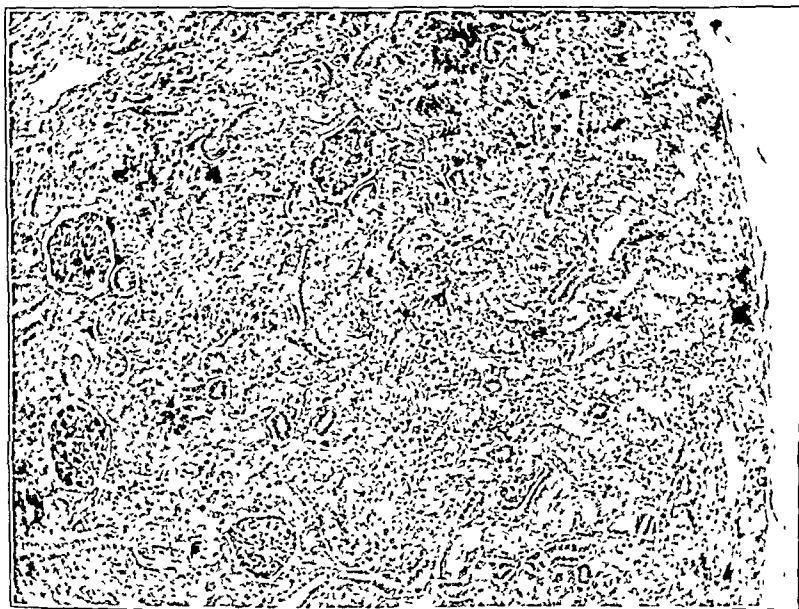


Fig. 7.—Cortex of right kidney of dog A 30, protocol 11. The right kidney was obstructed sixteen days, and two days following relief of the obstruction the left kidney was removed and the right kidney allowed a forty-two day repair period during which time it was forced to carry the entire renal function. There was no essential difference in the histologic appearance of this kidney as compared with the left; $\times 45$.

June 4: The right ureter was implanted into the bladder after a period of sixteen days of complete ureteral obstruction.

June 6: The blood urea was 23 mg.

June 6: Left nephrectomy was performed. The kidney appeared grossly normal and weighed 27.3 Gm. The measurements were: length, 5.1 cm.; transverse diameter, 3.5 cm.; anteroposterior diameter, 2.5 cm.; cortex, 8 mm.

June 8: The blood urea was 230 mg. per hundred cubic centimeters, but the general condition seemed good in spite of this high elevation.

On June 15, the blood urea was 127 mg.; June 24, 112 mg.; July 8, 72 mg. July 16: The dog was killed.

Necropsy.—The general observations were negative. The right kidney appeared somewhat small, and there was some definite dilatation of the ureter and pelvis still present. The weight and measurements were: weight, 22.3 Gm.; length, 5.5 cm.; transverse diameter, 3.1 cm.; anteroposterior diameter, 21 cm.; capacity of pelvis, 4.5 cc.; cortex, 6 mm. A pyelogram appeared normal except for a slight dilatation of the pelvis and ureter. The appearance of the kidneys is shown in figure 6.

Histologic Observations.—The kidneys showed no histologic abnormality and were identical in appearance except for a mild pyelonephritis and parenchymatous degeneration of tubular epithelium in the right kidney. Figure 7 shows the sub-capsular cortex of the right kidney. There were no atrophic, fibrosed glomeruli in the right kidney, nor was there any interstitial fibrosis.

PROTOCOL 12.—In dog A 48, a short haired, black and tan male mongrel, weighing 11.2 Kg., hydronephrosis was produced for nineteen days followed by a period of repair of thirty-four days.

July 1, 1925: The blood urea was 18.6 mg. per hundred cubic centimeters.

July 1: The right ureter was ligated.

July 20: The blood urea was 25.1 mg.

July 20: The right ureter was implanted into the bladder after a period of nineteen days of complete ureteral obstruction.

July 22: The blood urea was 21 mg.

July 27: Left nephrectomy was performed. The kidney appeared hypertrophied, but was otherwise normal. The weight and measurements were: weight, 47 Gm.; length, 6.6 cm.; transverse diameter, 3.9 cm.; anteroposterior diameter, 3.5 cm.; cortex, 7 mm.

August 4: The blood urea was 187.2 mg. The dog weighed 12.2 Kg.

August 23: The dog died from distemper.

Necropsy.—There were definite areas of consolidation in both lungs, but otherwise the results of the general necropsy were negative. The right kidney appeared somewhat large and showed definite dilatation of the pelvis and ureter. The anastomosis of the ureter into the bladder was patent. The weight measurements were: weight, 42.2 Gm.; length, 6.7 cm.; transverse diameter, 3.9 cm.; anteroposterior diameter, 2.6 cm.; cortex, 5.5 mm.; capacity of pelvis, 14 cc. A pyelogram showed that a fairly marked degree of hydronephrosis was still present (fig. 5). The gross appearance of the kidneys is shown in figure 6.

Histologic Observations.—Except for marked hyperemia there were no pathologic changes in the left kidney. The entire cortex and medulla of the right kidney showed a marked increase of interstitial fibrous connective tissue. This fibrosis did not have an even distribution but was most severe in the medulla and in the outer zones of the cortex with many dense radial scars. The glomeruli were condensed so that a great many were encountered in each field. Most of the glomerular tufts appeared normal as to structure although many of them were very small. They were uniformly hyperemic and in the corticomedullary zone a number of them were hypertrophic with collections of serum precipitate in the capsular spaces. Rarely small fibrosed glomeruli were seen. The tubules were generally very small in diameter, and occasional tubules were seen which were dilated and filled with red blood cells.

In this series of experiments (table 2), the right kidney was rendered hydronephrotic by complete ureteral obstruction for from eleven to nineteen days. Several days after the obstruction was relieved, the hypertrophic mate was removed so that the hydronephrotic kidney had to carry on all of the renal function.

While these experiments have no direct bearing on the question of renal atrophy of disuse, it was necessary to conduct them as control experiments in studying the problem of renal counterbalance, because, if it were demonstrated that an injured kidney did undergo progressive atrophy when allowed to remain in competition with its hypertrophic mate, it would also be essential to demonstrate that a similarly injured kidney could perform the necessary renal function if the entire load were

TABLE 2.—Data on Dogs with Repair of Hydronephrotic Kidney and Removal of Hypertrophic Mate

Protocol	Duration of Complete Obstruction of Right Ureter, Days	Interval Between Relief of Obstruction to Right Ureter and Left Nephrectomy, Days	Period of Repair of Right Kidney, Days	Weight of Kidneys, Gm.	
				Right, at Autopsy	Left, at Operation
6 (Dog A 20).....	11	2	828	58.2	34.5
7 (Dog A 33).....	15	2	505	32.0	38.0
8 (Dog A 40).....	15	2	293	40.6	36.7
9 (Dog A 24).....	12	2	155	34.1	30.9
10 (Dog A 38).....	16	3	79	44.5	45.1
11 (Dog A 30).....	16	2	42	22.3	27.3
12 (Dog A 48).....	19	7	34	42.2	47.0

thrown on it. In this way it could be indicated that the injury which had been applied to the kidney was not of itself sufficient to cause the progressive atrophy and that some other factor was necessary. These experiments show that the hydronephrotic kidney is capable of becoming a functionally good organ, and they are interesting in that they show how well an injured kidney can undergo repair and hypertrophy and carry on the entire renal function when the necessity is placed on it (figs. 5, 6 and 7).

In practically all these experiments the blood urea showed a definite elevation following the removal of the hypertrophic left kidney, but as a general rule this gradually returned to a relatively normal level. Apparently the injured right kidney could not immediately take over the entire load of renal function satisfactorily, but could do so later as it underwent repair and hypertrophy.

Histologically, the left kidneys of these animals were very hyperemic, and the glomerular tufts were plump and completely filled the capsular spaces. Occasional glomeruli contained collections of serum precipitate.

The right kidneys showed unmistakable glomerular hypertrophy which was especially well marked in those animals which were allowed the longest periods of repair after relief of the obstruction.

It would seem from the infrequency of finding damaged glomeruli or tubules even in as short a time as thirty-four days after relief of the obstruction that recovery from the injury is rapid when the entire functional load is placed on the injured kidney. This observation becomes particularly striking when the right kidneys of this series are compared with the right kidneys of series I. The only sign of injury manifested by the right kidneys of series II was diffuse interstitial fibrosis, and in animals having a repair period of forty-two days or more there was no evidence whatsoever of previous renal injury (fig. 7).

REPAIR OF THE HYDRONEPHROTIC KIDNEY WITH THE HYPERTROPHIC MATE UNDISTURBED

PROTOCOL 13.—In dog A, young black, male mongrel, weighing 12.8 Kg., hydronephrosis was produced for twelve days followed by a period of repair of eight hundred and seven days.

March 6, 1925: The preoperative blood urea was 30.5 mg. per hundred cubic centimeters. The right ureter was ligated.

On March 9, the blood urea was 43.2 mg.; March 13, 30.5 mg.; March 16, 18 mg. The dog was in excellent condition.

March 18: The right ureter was implanted into the bladder after a period of twelve days of complete ureteral obstruction.

On March 20, the blood urea was 41.6 mg.; March 25, 34 mg.; April 1, 27.2 mg.; April 16, 30 mg.; April 23, 40.2 mg.; May 7, 50 mg.; June 25, 30 mg.; July 22, 31.9 mg.; September 24, 40 mg.; October 16, 26 mg. (weight 24 Kg.); February 13, 1926, 46.8 mg.; March 17, 44.9 mg.; April 29, 26 mg.; June 3, 29.2 mg.; August 16, 28 mg.; October 13, 30 mg.; November 19, 36 mg.; Jan. 24, 1927, 47 mg.

On January 24, the microscopic examination of the urine was normal. On March 4, the blood urea was 32 mg.; on April 26, 30 mg.

June 3: The dog was first given 0.015 Gm. of morphine subcutaneously, and then 500 cc. of physiologic solution of sodium chloride was given intravenously in order to produce diuresis. With the animal under procaine hydrochloride anesthesia, the ureters were exposed and catheters were inserted into them. One cubic centimeter of phenolsulphonphthalein was given intravenously. On the left side the appearance time was four minutes, and 44 per cent of the dye was excreted in one hour in 20 cc. of urine. On the right side the appearance time was eight minutes, and 14 per cent of the dye was excreted in one hour in 14 cc. of urine. The urine from each kidney was normal. The dog was killed with magnesium sulphate injected intravenously.

Necropsy.—The dog weighed 23.2 Kg. All the organs were normal except the kidneys. The right kidney was about one-half the size of the left, but had the appearance of a functioning organ with a firm parenchyma. The anastomosis between the right ureter and the bladder was patent. The right ureter showed a moderate degree of dilatation, and there was a rather marked degree of dilatation of the extrarenal portion of the pelvis of the right kidney. The left kidney

appeared to be normal and somewhat hypertrophied. The weights and measurements of the kidneys were:

	Right	Left
Weight	40.5 Gm.	71.5 Gm.
Length	6.6 cm.	7.5 cm.
Transverse diameter.....	3.8 cm.	4.5 cm.
Anteroposterior diameter.....	2.2 cm.	2.5 cm.
Capacity of pelvis.....	12.0 cc.	5.0 cc.
Cortex	5.0 mm.	5.5 mm.

The appearance of the kidneys is shown in figure 8. Pyelograms of both kidneys were made (fig. 9). The pyelogram of the right kidney showed a marked dilatation of the extrarenal portion of the pelvis, but the intrarenal portion of the pelvis and the calices appeared to be relatively normal. The pyelogram of the left kidney was normal.

Histologic Observations.—The right and left kidneys were histologically identical except that the glomeruli were uniformly hypertrophic in the right. Occasional fibrosed tufts adherent to thickened capsules were seen in both kidneys, but neither showed any interstitial fibrosis nor any evidence of extensive glomerular or tubular atrophy (fig. 10).

PROTOCOL 14.—In dog A 41, a red and brown female, weighing 8.8 Kg., hydro-nephrosis was produced for sixteen days followed by a period of repair of seven hundred and twenty-eight days.

May 18, 1925: The blood urea was 41.6 mg. per hundred cubic centimeters.

May 19: The right ureter was ligated.

On May 21, the blood urea was 23.5 mg., and on May 25, 35.1 mg.

June 4: The right ureter was implanted into the bladder after a period of sixteen days of complete ureteral obstruction.

On June 6, the blood urea was 29 mg.; June 15, 38.6 mg.; June 24, 35 mg.; July 8, 29.5 mg. (general condition good, weight 8.2 Kg.); July 31, 28.9 mg.; September 24, 20 mg.; October 16, 27 mg.; November 13, 33 mg.; Jan. 14, 1926, 46.8 mg.; March 17, 25.1 mg.; April 29, 22 mg.; June 3, 36.4 mg.; June 24, 44 mg.; August 16, 22 mg.; October 13, 20 mg.; November 19, 27 mg. On December 23, the microscopic examination of urine was normal. On Jan. 24, 1927, the condition of the dog was good, and blood urea was 35 mg. On March 4, it was 22 mg., and on April 26, 24 mg.

June 2: The dog was given 0.015 Gm. of morphine, subcutaneously, and 500 cc. of water was given by stomach tube to produce diuresis. With the animal under procaine hydrochloride anesthesia, both ureters were exposed and catheters were inserted into them. One cubic centimeter of phenolsulphonphthalein was injected intravenously. On the left side the appearance time was four minutes, and 50 per cent of the dye was excreted in one hour in 18 cc. of urine. On the right side the appearance time was fifteen minutes, and 10 per cent of the dye was excreted in 8 cc. of urine in one hour. The urine from each kidney was normal. The dog was killed with ether.

Necropsy.—The dog weighed 13.8 Kg. All the organs were normal except the kidneys. The right kidney was small and somewhat atrophic. The lower pole was somewhat larger than the upper one. The parenchyma was firm and seemed to consist of good renal tissue. The anastomosis between the right ureter and the bladder was patent. The right ureter showed a moderate degree of dilatation, but the kidney itself was not hydronephrotic. The left kidney appeared to be

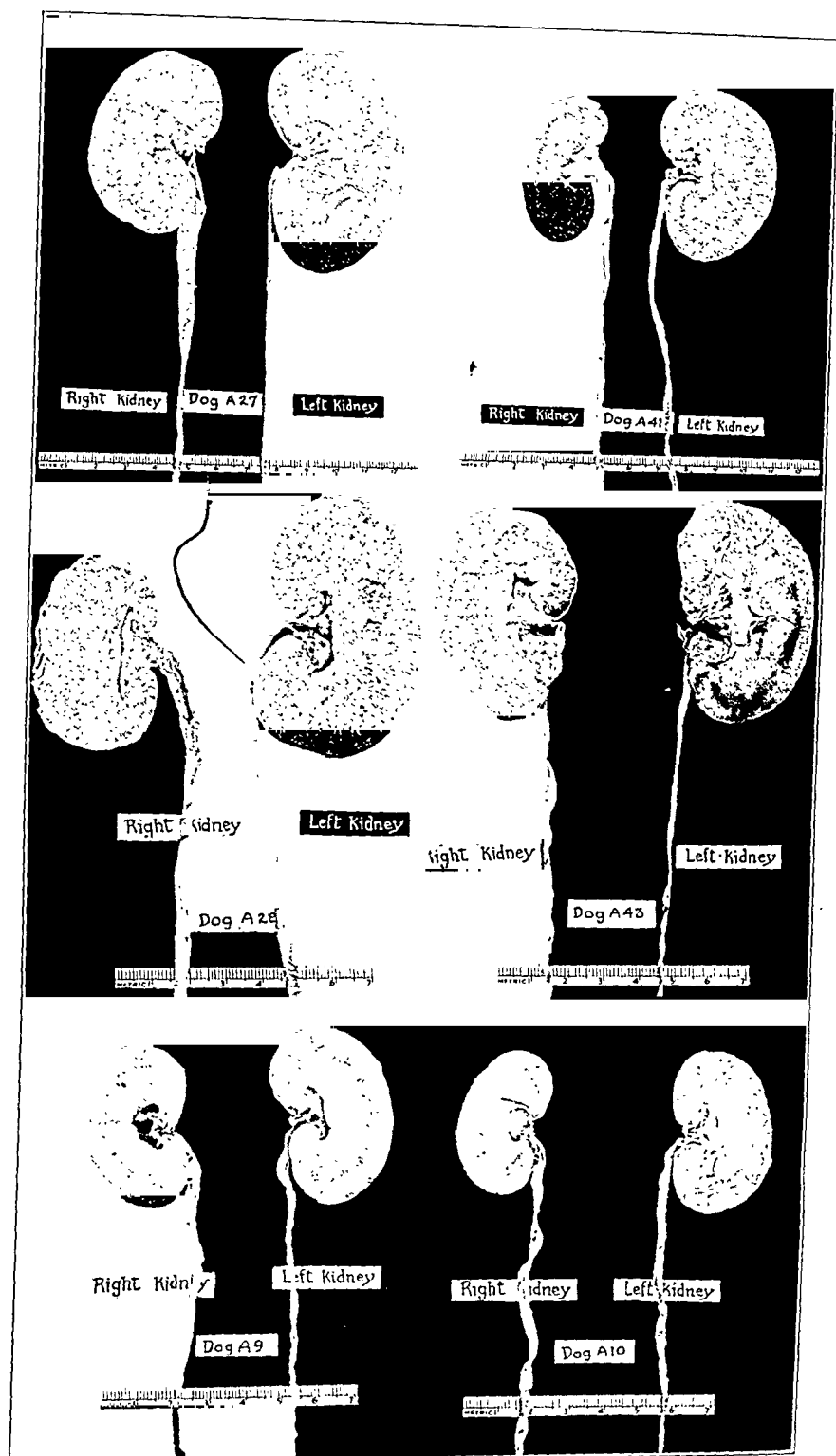


Fig. 8 A and B.—Appearance of kidneys in experiments of group III. The right ureter had been obstructed for periods varying from twelve to nineteen days following which the obstruction was relieved and the right kidney allowed to function in "competition" with its undisturbed hypertrophic mate. These photographs show that the right kidneys contain a considerable amount of renal tissue and did not undergo atrophy of disuse (table 3).

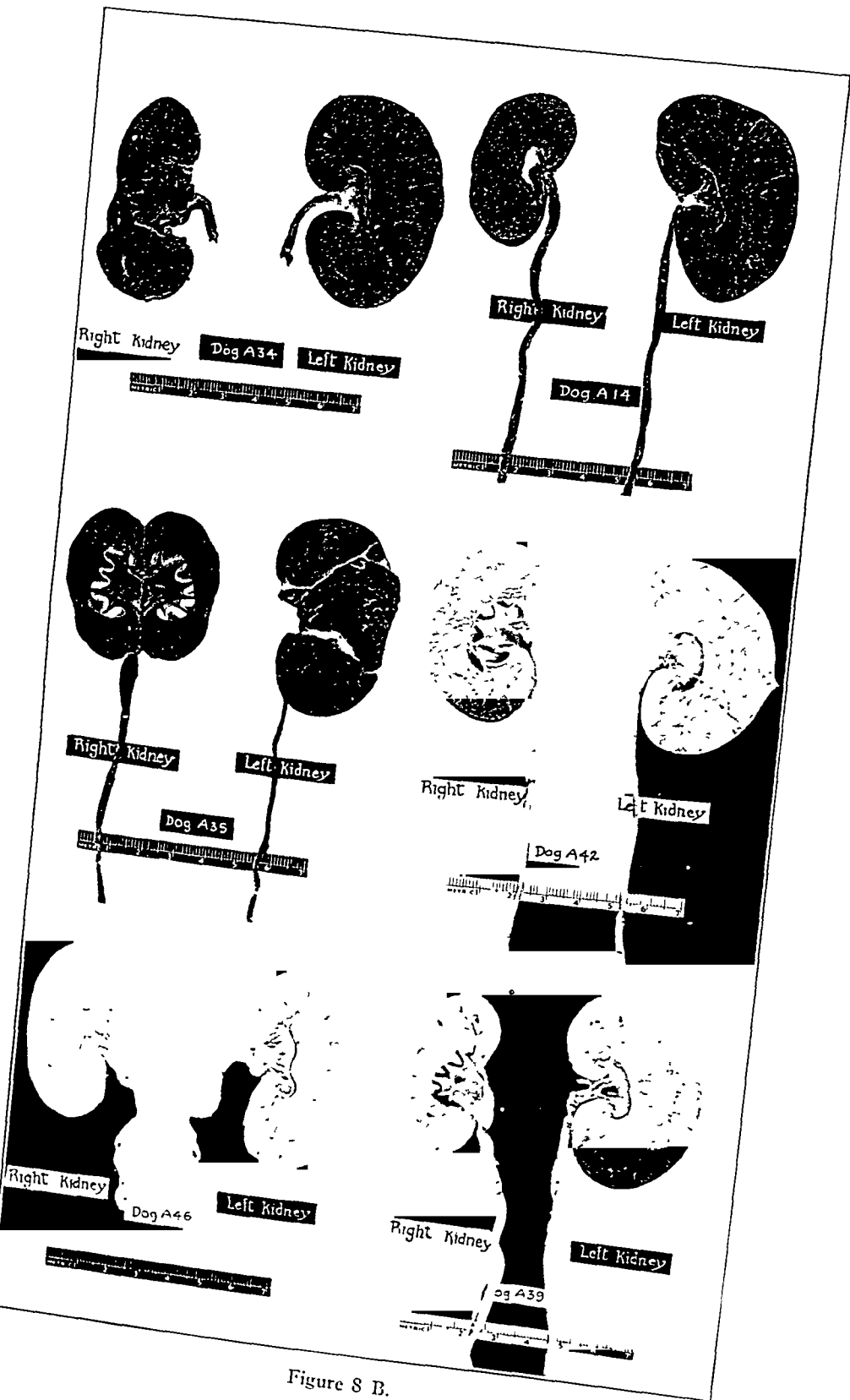


Figure 8 B.

normal and somewhat hypertrophied. The weights and measurements of the kidneys were:

	Right	Left
Weight	16.2 Gm.	48.7 Gm.
Length	5.2 cm.	6.4 cm.
Transverse diameter.....	2.5 cm.	4.1 cm.
Anteroposterior diameter.....	1.9 cm.	3.5 cm.
Capacity of pelvis.....	5.5 cc.	3.5 cc.
Cortex	3.0 mm	6.0 mm

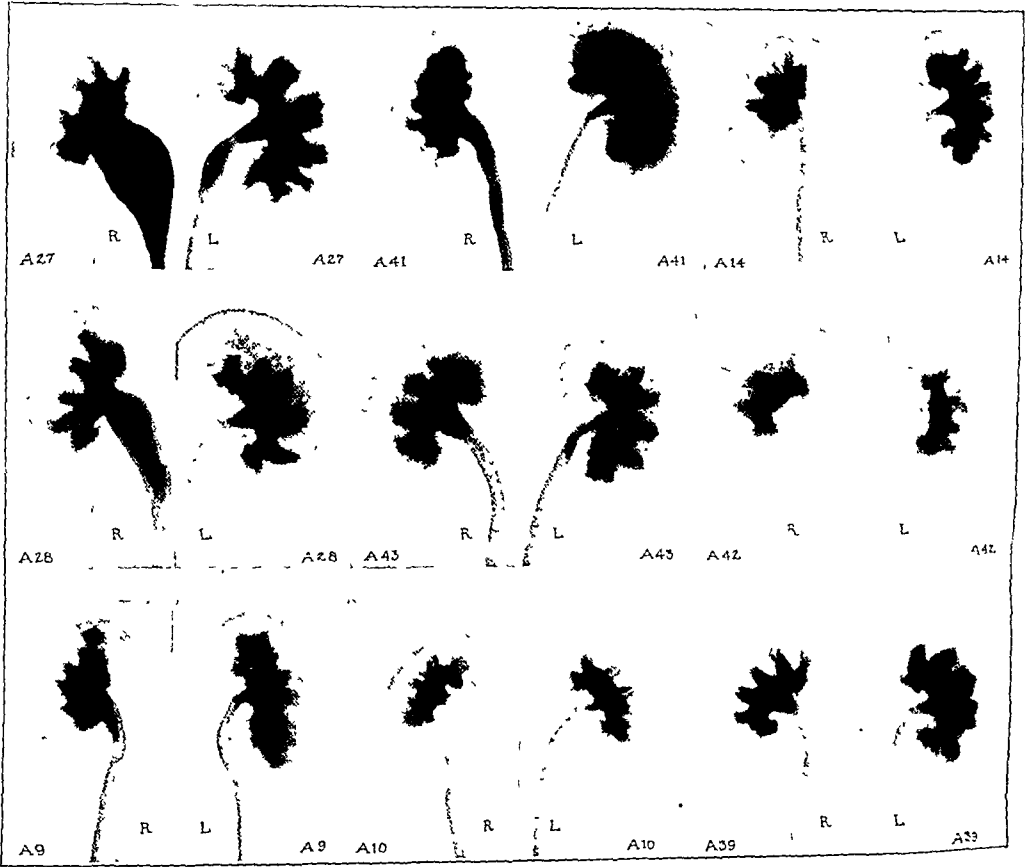


Fig. 9.—Pyelograms of the right and left kidneys of the experiments of group III. These show a tendency of the hydronephrotic pelvis to return to normal although the ureter frequently remained dilated.

The appearance of the kidneys is shown in figure 8.

Pyelograms were made of each kidney (fig. 9). Except for the dilatation of the ureter and extrarenal portion of the pelvis and some extravasation of the sodium iodide in the region of the upper pole, the pyelogram of the right kidney was essentially normal. The pyelogram of the left kidney showed nothing abnormal.



Fig 10.—Sections from the cortex of the right and left kidneys of dog A 27, protocol 13. The right kidney was obstructed for sixteen days and then allowed a repair period of eight hundred seven days, working in "competition" with the undisturbed left kidney. There were no important histologic differences between the right and left kidneys; $\times 65$. *A* indicates the right kidney; *B*, the left.

Histologic Observations.—A few hyalinized glomeruli were present in the left kidney, and many of the glomeruli contained a small amount of serum precipitate within the capsular spaces. Hyaline tubular casts were frequent. In one slide a small abscess was seen in the cortex just beneath the capsule.

In the right kidney, the cortex corticis had entirely disappeared and occasional glomeruli were seen in the most peripheral portions of the cortex. Just beneath the capsule there were a number of thin scars which showed a moderately dense lymphocytic infiltration. These scars ran parallel to the capsule for distances as great as 5 mm., but did not extend more than from 60 to 80 microns into the cortex and probably represented the atrophied cortex corticis. The cortex proper was greatly reduced in thickness, but except for the scarring just described there were no histologic differences in the right and left kidneys of this animal. There was no increase either in the number of atrophic glomeruli or of interstitial fibrous connective tissue.

PROTOCOL 15.—In dog A 34, a female mongrel, weighing 10.8 Kg., hydro-nephrosis was produced for fifteen days followed by a period of repair of four hundred and sixty-five days.

May 18, 1925: The preoperative blood urea was 36.1 mg. per hundred cubic centimeters.

May 25: The right ureter was ligated.

On May 27, the blood urea was 43.2 mg.; on June 9, 43.2 mg.

June 9: The right ureter was implanted into the bladder after a period of fifteen days of complete ureteral obstruction.

On June 11, the blood urea was 35 mg.; June 15, 43 mg.; June 24, 45 mg.; July 8, 48.8 mg. (weight 10.2 Kg. and general condition excellent); July 31, 34.5 mg.; September 24, 25 mg.; October 16, 18.7 mg.; November 13, 17.5 mg.; Feb. 13, 1926, 31 mg.; March 17, 25.3 mg.; April 29, 39 mg.

September 16: The dog was killed, and a complete autopsy was not performed; only the kidneys were preserved. The right kidney was definitely smaller than the left. The greatest amount of parenchyma was found to be situated in the regions of the upper and lower poles, the central portion of the kidney suggesting an atrophic condition. The hilum was enlarged, and the ureter and pelvis were dilated. The left kidney was a normal hypertrophic organ. The weights and measurements of the kidneys were:

	Right	Left
Weight	15.0 Gm.	45.0 Gm.
Length	6.0 cm.	6.3 cm.
Transverse diameter.....	2.8 cm.	4.0 cm.
Anteroposterior diameter.....	1.4 cm.	3.1 cm.
Cortex	2.0 mm.	6.0 mm.

The appearance of the kidneys is shown in figure 8.

Histologic Observations.—Except for the reduction in the thickness of the cortex of the left, there were no histologic differences in the two kidneys. Both were the seat of a mild chronic pyelonephritis, and the radial areas of cortical inflammation contained many atrophic glomeruli and tubules and were densely fibrosed and infiltrated by leukocytes and lymphocytes. Both kidneys showed areas in which the entire width of cortex and medulla appeared normal.

PROTOCOL 16.—In dog A 14, a short haired, male mongrel, weighing 7.8 Kg., hydronephrosis was produced for sixteen days followed by a period of repair of three hundred and sixty-two days.

Dec. 8, 1924, the blood urea was 28 mg. per hundred cubic centimeters.

December 11: The blood urea was 187 mg. The right ureter was ligated.

On December 13, the blood urea was 262 mg.; on December 23, 31.2 mg.

December 23: The right ureter was implanted into the bladder after a period of twelve days of complete ureteral obstruction.

On December 26, the blood urea was 33.5 mg.; Jan. 6, 1925, 27 mg.; January 13, 31.2 mg.; January 27, 26.5 mg. (weight 9.4 Kg. and general condition good); February 13, 267 mg.; February 26, 47 mg.; March 9, 35.1 mg.; March 16, 26 mg.; March 25, 41.6 mg.; April 1, 37.3 mg.; April 10, 25.5 mg.; April 16, 37.4 mg.; May 7, 49 mg.; June 25, 27 mg. (weight 10.8 Kg.); July 22, 23.5 mg.; October 16, 33 mg.; November 13, 40 mg.

December 20: The dog was found dead. Necropsy showed the presence of bilateral pneumonia but the other organs, excepting the kidneys, were normal. The right kidney was definitely smaller than the left, but showed grossly normal parenchyma. The right ureter was not dilated and the anastomosis between the ureter and bladder was patent. The left kidney was a normal hypertrophied organ. The urine which was obtained from the bladder showed no abnormalities. The weights and measurements of the kidneys were:

	Right	Left
Weight	14.1 Gm	44.2 Gm
Length	4.7 cm	6.4 cm
Transverse diameter	2.4 cm	3.7 cm
Anteroposterior diameter	1.6 cm	3.0 cm
Capacity of pelvis	2.0 cc	3.0 cc.
Cortex ..	4.0 mm	8.0 mm

The appearance of the kidneys is shown in figure 8

Pyelograms showed the right kidney and pelvis to be smaller than the left, but otherwise no definite abnormalities were seen (fig. 9).

Histologic Observations.—Except for a slight patchy pyelonephritis and the presence of serum precipitate in the glomeruli, the left kidney showed no pathologic change.

The capsule of the right kidney showed irregular thickening, and the cortex corticis had entirely disappeared. There was a wide zone of interstitial fibrosis in the outer portion of the cortex with short radial extensions at intervals toward the medulla. In this fibrosed zone the glomeruli were concentrated. The glomeruli themselves were small, fibrosed and often hyalinized, and associated with them were many atrophic contracted tubules. Deeper in the cortex proper both glomeruli and tubules appeared normal and here there was no increase in interstitial fibrous connective tissue. The medulla showed patchy areas of fibrosis. This kidney was also the seat of a very mild pyelonephritis.

Protocol 17.—In dog A 28, white male terrier, weighing 14.4 Kg., hydro-nephrosis was produced for twelve days followed by a period of repair of two hundred and seventeen days.

March 6, 1925: The preoperative blood urea was 50 mg. per hundred cubic centimeters. The right ureter was ligated.

On March 9, the blood urea was 60 mg.; March 13, 50 mg.; March 16, 26 mg.

March 18: The right ureter was implanted into the bladder after a period of twelve days of complete ureteral obstruction.

On March 20, the blood urea was 43.2 mg.; March 25, 36.4 mg.; April 1, 42.2 mg.; April 16, 36 mg.; June 25, 43 mg.; July 22, 48.4 mg.; September 24, 43.2 mg.; October 16, 16 mg. (general condition good).

October 21: The dog was killed.

Necropsy.—All the viscera were normal except the kidneys. The right kidney showed a firm parenchyma but was only about one-half as large as the left kidney. The right ureter was somewhat dilated as was also the extrarenal portion of the pelvis. The anastomosis between the right ureter and the bladder was patent. The left kidney was a normal hypertrophied organ. The weights and measurements of the kidneys were:

	Right	Left
Weight	31.5 Gm.	69.2 Gm.
Length	5.3 cm.	6.6 cm.
Transverse diameter.....	3.3 cm.	4.4 cm.
Anteroposterior diameter.....	2.7 cm.	3.9 cm.
Capacity of pelvis.....	6.5 cc.	5.5 cc.
Cortex	4.0 mm.	8.0 mm.

The appearance of the kidneys is shown in figure 8.

Pyelograms were made of each kidney (fig. 9). These showed the right kidney to be smaller than the left with a definite dilatation of its ureter and the extrarenal portion of its pelvis, but the intrarenal portion of its pelvis appeared relatively normal. The pyelogram of the left kidney was normal.

Histologic Observations.—A few fibrosed and hyalinized glomeruli with thickened capsules were seen in the left kidney; otherwise it showed no pathologic change.

There was an irregular thickening of the capsule of the right kidney, beneath which a narrow zone of the cortex showed marked interstitial fibrosis. In this zone there was a concentration of glomeruli and tubules showing many stages of atrophy up to complete obliteration. Some of the glomeruli showed marked reduction in the size of the tufts without reduction in the size of the capsule so that there remained a large empty space between the capsule and tuft. Occasional small capsules were seen in which the tuft had entirely disappeared. There were small radial extensions of this peripheral zone of fibrosis toward the medulla. A wide inner zone of the cortex and the corticomedullary zone appeared entirely normal. There was some radial scarring of the medulla. Figure 11 shows the fibrosed peripheral zone of the cortex and the deeper unchanged zone.

PROTOCOL 18.—In dog A 43, long haired, female mongrel, weighing 14.8 Kg., hydronephrosis was produced for thirteen days followed by a period of repair of one hundred and fifty-four days.

The preoperative blood urea was 27 mg. per hundred cubic centimeters.

June 17, 1925: The right ureter was ligated.

On June 25, the blood urea was 30 mg.; on June 30, 34 mg.

June 30: The right ureter was implanted into the bladder after a period of thirteen days of complete ureteral obstruction.

July 8: The condition of the dog was good. She weighed 14.6 Kg., and the blood urea was 30.3 mg.

On July 31, the blood urea was 24 mg.; September 24, 22 mg.; October 16, 25 mg.; November 13, 31 mg.

December 1: The dog died after an apparent illness of a few weeks.

Necropsy.—There were no external signs of injury. There was a thick purulent exudate throughout the mediastinum. The pleural cavities and lungs were not involved. The esophagus showed no perforations, nor did the trachea or large bronchi. The source of the infection was undetermined. The heart and pericardium were normal. All abdominal organs except the kidneys were normal. The right kidney was slightly smaller than the left. Its ureter and pelvis showed

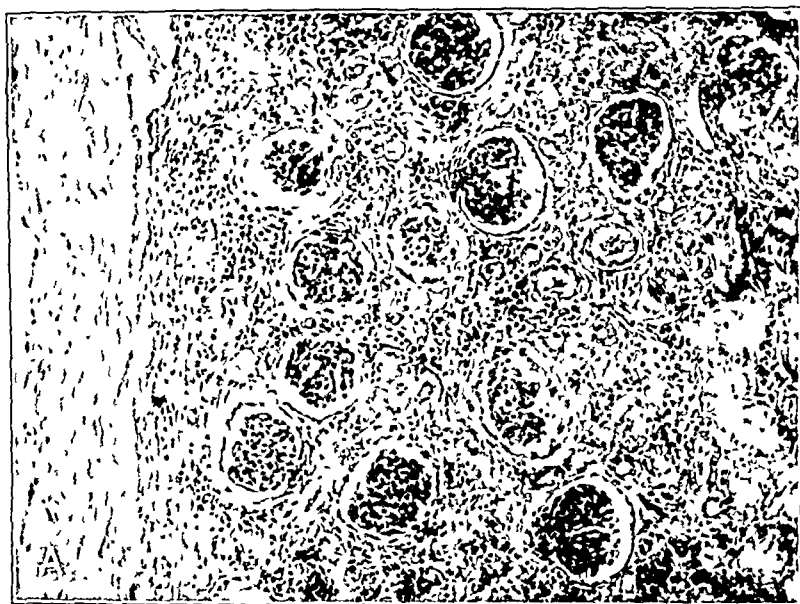


Fig 11.—Cortex of the right kidney of dog A 28, protocol 17. The kidney had been obstructed for twelve days and allowed a repair period of two hundred seventeen days in "competition" with its undisturbed mate. *A* shows the fibrosed peripheral zone of the cortex, with atrophic tubules and concentration of glomeruli; *B*, the deeper layer of the cortex in which there was no atrophy or interstitial fibrosis; $\times 60$.

a slight degree of dilatation, but the kidney was otherwise grossly normal. The anastomosis between the right ureter and the bladder was patent. The left kidney appeared to be normal. The weights and measurements of the kidneys were:

	Right	Left
Weight	38.1 Gm.	44.2 Gm.
Length	5.9 cm.	6.1 cm.
Transverse diameter.....	4.0 cm.	3.8 cm.
Anteroposterior diameter.....	2.2 cm.	3.0 cm.
Capacity of pelvis.....	5.0 cc.	5.5 cc.
Cortex	6.0 mm.	7.0 mm.

The appearance of the kidneys is shown in figure 8.

Pyelograms of both kidneys were made (fig. 9). Aside from the slight dilatation of the right ureter, no remarkable difference between the two sides was noted.

Histologic Observations.—Except for a reduction of the thickness of the cortex with radial scarring of the medulla of the left kidney, there was no histologic difference between the two kidneys of this animal.

PROTOCOL 19.—In dog A 35, a brown and white female mongrel, weighing 10.2 Kg., hydronephrosis was produced for sixteen days followed by a period of repair of ninety-one days.

May 18, 1925: The blood urea was 29 mg. per hundred cubic centimeters.

May 20: The right ureter was ligated.

On May 25, the blood urea was 41 mg.; on June 3, 43.2 mg.

June 5: The right ureter was implanted into the bladder after a period of sixteen days of complete ureteral obstruction.

On June 8, the blood urea was 48.8 mg.; June 15, 42 mg.; June 24, 42 mg.; July 8, 27.6 mg.; July 31, 26.1 mg. The dog appeared weak and mangy, and weighed 6.8 Kg. on July 8.

September 4: The dog was killed in a fight.

Necropsy.—There was a wound in the chest which opened into the left pleural cavity and also a wound of the left lumbar region through which the left kidney had been lacerated. The dog was somewhat emaciated. The right kidney was small and firm. The anastomosis between the right ureter and the bladder was patent. There was some dilatation of the right ureter and renal pelvis. The left kidney was lacerated, but otherwise seemed to be a normal hypertrophied organ. The weights and measurements of the kidneys were:

	Right	Left
Weight	11.8 Gm.	28.7 Gm.
Length	4.7 cm.	6.7 cm.
Transverse diameter.....	2.7 cm.	3.1 cm.
Anteroposterior diameter.....	1.5 cm.	2.4 cm.
Cortex	2.0 mm.	5.0 mm.

The appearance of the kidneys is shown in figure 8.

The pyelogram of the right kidney showed a rather small organ. The ureter and renal pelvis showed some dilatation but this was not marked.

Histologic Observations.—The left kidney showed no abnormality on histologic examination.

The right kidney showed a complete disappearance of the cortex corticis with a thickened capsule. The capsular thickening was irregular and occasional prolongation of the fibrous connective tissue extended down into the underlying cortex. Only a narrow zone of the cortex adjacent to the medulla contained normal glomeruli and tubules and was comparatively free from the interstitial fibrosis

which invaded most of the cortex and medulla. Here again there was a concentration of atrophic glomeruli in the peripheral zone of the cortex. There was a mild degree of pyelonephritis.

PROTOCOL 20.—In dog A 42, a brindle male mongrel, weighing 13.6 Kg., hydro-nephrosis was produced for thirteen days, followed by a period of repair of seventy-eight days.

The preoperative blood urea was 18 mg. per hundred cubic centimeters.

June 17, 1925: The right ureter was ligated.

On June 25, the blood urea was 53 mg.; on June 30, 42 mg.

June 30: The right ureter was implanted into the bladder after a period of thirteen days of complete ureteral obstruction.

July 8: The blood urea was 67.6 mg., and the weight, 12.5 Kg. The general condition of the dog was good.

July 31: The blood urea was 24.9 mg.

September 16: The dog was killed.

Necropsy.—The organs were essentially normal except the kidneys. The right kidney was smaller than the left but it consisted of normal firm parenchyma. The right ureter and pelvis showed slight dilatation. The anastomosis between the right ureter and the bladder was patent. The left kidney was a normal hypertrophied organ. The weights and measurements of the kidneys were:

	Right	Left
Weight	28.8 Gm.	38.3 Gm.
Length	5.4 cm.	6.0 cm.
Transverse diameter.....	2.9 cm.	3.3 cm.
Anteroposterior diameter.....	2.1 cm.	2.8 cm.
Capacity of pelvis.....	7.0 cc.	2.4 cc.
Cortex	5.0 mm.	7.0 mm.

The appearance of the kidneys is shown in figure 8.

Pyelograms of both kidneys showed a mild degree of dilatation of the right ureter and pelvis, but no other remarkable changes were noted (fig. 9).

Histologic Observations.—There was no histologic difference between the right and the left kidneys except the reduction in width of the cortex of the right kidney.

PROTOCOL 21.—In dog A 9, a mongrel poodle, weighing 8 Kg., hydronephrosis was produced for twelve days followed by a period of repair of seventy-one days.

On Nov. 13, 1924, the blood urea was 37.4 mg.; on November 14, 26.6 mg.

December 5: The right ureter was ligated.

On December 8, the blood urea was 26.1 mg.; December 11, 32.4 mg.; December 13, 46 mg.

December 17: The right ureter was implanted into the bladder after a period of twelve days of complete ureteral obstruction.

On December 23, the blood urea was 46.8 mg.; December 26, 48.5 mg.; Jan. 6, 1925, 37.4 mg.; January 13, 39.2 mg.; January 27, 35.5 mg. (weight, 5.5 Kg.); February 3, 41.6 mg.; February 13, 43 mg. (weight, 5.3 Kg.). The dog developed mange on February 13.

February 26: The blood urea was 67.4 mg. The mange was severe and the general condition was poor. The dog was killed with ether.

Necropsy.—There was some consolidation in the lower lobe of each lung. The liver, spleen, pancreas and adrenals were normal. The small intestine was found to contain a large number of worms. The right kidney was somewhat smaller than the left. The right ureter and pelvis were dilated. The parenchyma of the right kidney was firm and grossly appeared to be normal. The anastomosis

between the right ureter and the bladder was patent. The left kidney was normal. The weights and measurements of the kidneys were:

	Right	Left
Weight	16.0 Gm.	22.0 Gm.
Length	4.6 cm.	5.1 cm.
Transverse diameter.....	2.7 cm.	3.1 cm.
Anteroposterior diameter.....	1.7 cm.	2.3 cm.
Capacity of pelvis.....	3.0 cc.	2.5 cc.
Cortex	4.5 mm.	5.0 mm.

The appearance of the kidney is shown in figure 8.

Pyelograms were made of both kidneys (fig. 9), and aside from the slight dilatation of the right ureter and pelvis no abnormalities were seen in either pyelogram.

Histologic Observations.—There was no histologic difference between the right and left kidneys except the reduction in the cortex of the right kidney.

PROTOCOL 22.—In dog A 10, a short haired, brown female mongrel, weighing 5.5 Kg., hydronephrosis was produced for thirteen days followed by a period of fifty-six days.

The preoperative blood urea was 30 mg. per hundred cubic centimeters.

Dec. 6, 1924: The right ureter was ligated.

On December 8, the blood urea was 56.1 mg.; December 11, 50.1 mg.; December 13, 57 mg.

December 19: The right ureter was implanted into the bladder after a period of thirteen days of complete ureteral obstruction.

On December 23, the blood urea was 59.1 mg.; December 26, 56 mg.; Jan. 13, 1925, 41.6 mg.; January 27 (weight, 5.7 Kg., and general condition good); February 3, 50.6 mg.; February 13, 60.5 mg.

February 13: The dog was killed. She weighed 5.9 Kg.

Necropsy.—The organs were essentially normal except the kidneys. The right kidney was somewhat smaller than the left; the parenchyma was firm; the ureter and pelvis were slightly dilated. The anastomosis between the right ureter and the bladder was patent. The left kidney was normal and somewhat hypertrophic. The weights and measurements of the kidneys were:

	Right	Left
Weight	9.7 Gm.	15.4 Gm.
Length	3.9 cm.	4.8 cm.
Transverse diameter.....	2.2 cm.	2.6 cm.
Anteroposterior diameter.....	1.5 cm.	2.2 cm.
Capacity of pelvis.....	4.0 cc.	3.5 cc.
Cortex	4.0 mm.	4.0 mm.

The appearance of the kidneys is shown in figure 8.

Pyelograms were made of both kidneys (fig. 9), and these were found to be normal except for the dilatation of the right ureter.

Histologic Observations.—The left kidney showed no abnormality on histologic examination other than a mild pyelonephritis.

The right kidney showed a diffuse interstitial fibrosis most marked in the subcapsular zone of the cortex. The capsule was thickened and there was a concentration of glomeruli immediately beneath it. Some of the glomeruli appeared normal and occasional groups of normal appearing tubules extended up into the densely fibrosed cortex corticis. There was a diffuse atrophy of both tubules and glomeruli. Deeper in the cortex there were many radially disposed scars and occasional atrophic glomeruli. The medulla showed a patchy increase of fibrous connective tissue. There was a mild pyelonephritis.

PROTOCOL 23.—In dog A 46, a black and brown male mongrel, weighing 12.6 Kg., hydronephrosis was produced for nineteen days followed by a period of repair of forty-three days.

The preoperative blood urea was 36 mg. per hundred cubic centimeters.

July 1, 1925: The right ureter was ligated.

July 20: The blood urea was 44.2 mg. The right ureter was implanted into the bladder after a period of nineteen days of complete ureteral obstruction.

On July 22, the blood urea was 43.2 mg.; July 27, 53.5 mg.; August 4, 45.6 mg. (weight, 12.6 Kg.); August 13, 36.1 mg.

September 1: The dog was killed.

Necropsy.—Only the kidneys were preserved at autopsy. The right kidney was definitely smaller than the left but the parenchyma was firm and grossly appeared normal. There was a slight dilatation of the right ureter and pelvis of the right kidney. The left kidney was a normal hypertrophied organ. The weights and measurements of the kidneys were:

	Right	Left
Weight	19.5 Gm.	41.0 Gm.
Length	5.5 cm.	6.3 cm.
Transverse diameter.....	2.4 cm.	3.5 cm.
Anteroposterior diameter.....	2.0 cm.	3.4 cm.
Cortex	5.0 mm.	7.0 mm.

The appearance of the kidneys is shown in figure 8.

Histologic Observations.—Left Kidney: No pathologic changes were noted.

In the right kidney, there was a slight diffuse increase in the interstitial fibrous connective tissue throughout the kidney. This fibrosis was most marked in the cortex corticis and the outer zone of the cortex proper. Here there were a number of fine radial scars, broadest at the capsule and extending toward the medulla. In the vicinity of the scars there was considerable atrophy of both tubules and glomeruli, many of the latter being fibrotic. In general, however, the glomerular tufts were plump and cellular. The glomeruli were smaller and approximated one another more closely than in the left kidney.

PROTOCOL 24.—In dog A 39, a brown and white female mongrel, weighing 8.6 Kg., hydronephrosis was produced for sixteen days followed by a period of repair of twenty-four days.

May 18, 1925: The blood urea was 30.5 mg. per hundred cubic centimeters.

May 20: The right ureter was ligated.

On May 25, the blood urea was 30.3 mg.; on June 3, 48.3 mg.

June 5: The right ureter was implanted after a period of sixteen days of complete ureteral obstruction.

On June 8, the blood urea was 41.6 mg.; June 15, 32 mg.; June 24, 34 mg.

June 29: The dog was killed.

Necropsy.—All the organs were normal except the kidneys. The right kidney was definitely smaller than the left and showed some dilatation of the pelvis and ureter. The parenchyma was firm. The anastomosis between the right ureter and the bladder was patent. The left kidney was a normal hypertrophied organ. The weights and measurements of the kidneys were:

	Right	Left
Weight	17.6 Gm.	40.4 Gm.
Length	5.0 cm.	6.2 cm.
Transverse diameter.....	2.7 cm.	4.1 cm.
Anteroposterior diameter.....	1.8 cm.	2.8 cm.
Cortex	3.0 mm.	6.0 mm.
Capacity of pelvis.....	3.5 cc.	4.0 cc.

The appearance of the kidneys is shown in figure 8.

Pyelograms were made of both kidneys (fig. 9). The right kidney appeared definitely smaller than the left and its ureter was slightly dilated, but aside from these changes the two kidneys appeared to be normal.

Histologic Observations.—The glomeruli in the left kidney were large and the tufts plump, in most instances filling their capsules. The organ was very hyperemic, many of the interlobular vessels being greatly distended.

There was marked tubular atrophy of the right kidney with degeneration of tubular epithelium. The atrophy was particularly severe in the cortex corticis and in the outer zone of the cortex proper giving this part of the kidney a compact appearance with concentration of glomeruli. There were many instances of tubular epithelial regeneration, and the regenerated tubules stood out in sharp contrast to the collapsed atrophic ones. Many of the glomeruli in the zone of the cortex had capsules of normal size but only a small portion of the tufts still intact. The greater part of such a glomerular tuft was represented by a granular basophilic mass containing a few fragmented and pyknotic nuclei lying free in the capsular space. Deeper in the cortex there were many normal appearing glomeruli, but here as well as in the medulla there were many collapsed tubules with degenerated epithelium.

In these experiments, which bear more directly on the subject of renal atrophy of disuse, the right kidney was injured by the production of a complete ureteral obstruction which existed in the various experiments from twelve to nineteen days. After the obstruction was relieved, the injured right kidney was placed "in competition" with the hypertrophic left kidney, and this period extended from twenty-four to eight hundred and seven days. According to Hinman's theory, the right kidney was thus placed at a distinct disadvantage, first because of the injury itself and secondly because its mate had become hypertrophied and accustomed to having the entire demand for renal function placed on it.

The important questions which arise concerning the fate of the right kidney are as follows: Does it undergo progressive atrophy and become a functionless and worthless organ? What are the gross and histologic changes that take place in it?

In the early part of the "competitive period" we must expect some rapid changes to occur in the right kidney. With relief of the obstruction the kidney soon changes from a large dilated structure to a considerably smaller and firmer organ. The ureter and extrarenal portion of the pelvis frequently remain permanently dilated, but the dilatation of the intrarenal portion of the pelvis may entirely disappear as in dog A 28, protocol 17 (figs. 8 and 9). In no experiment did the atrophy approach completeness and, in fact, there is no conclusive evidence that any atrophy occurred following the release of the hydronephrotic pressure. From our histologic studies it would appear that during the period of ureteral obstruction numerous uriniferous units (tubules and glomeruli) were either destroyed or so severely damaged that necrosis

followed in spite of the removal of the obstruction. These damaged units gradually disappeared, and with their disappearance there developed considerable interstitial fibrosis, and within a period of ten or eleven weeks even the fibrous tissue had disappeared. It seems possible that this gradual but complete disappearance of these injured uriniferous units may account for the smaller relative size of the right kidney in some of those experiments in which there was a long period of repair rather than a true progressive atrophy of disuse.

The right kidney from dog A 27, protocol 13, seemed to be a functioning organ and by weight made up 36 per cent of the total renal mass even though the period of "competition" had lasted eight hundred and seven days. Both grossly and microscopically (figs. 8 and 10), this kidney consisted of tissue which was important, if not for active function, certainly as renal reserve. The excretion of phenolsulphonphthalein by this kidney was 14 per cent in 14 cc. of urine in one hour with an appearance time of eight minutes. The left kidney excreted 44 per cent of the dye in 20 cc. of urine with an appearance time of four minutes. The right kidney in dog A 41, protocol 14, constituted only 25 per cent of the total renal mass, but it had not undergone complete atrophy even though its ureter had been completely obstructed for sixteen days and the kidney had remained in "competition" with its hypertrophied mate for seven hundred and twenty-eight days. This injured kidney excreted only 10 per cent of phenolsulphonphthalein in 8 cc. of urine in one hour with an appearance time of fifteen minutes. The left kidney excreted 50 per cent of the dye in 18 cc. of urine in one hour with an appearance time of four minutes. The right kidney of dog A 34, protocol 15, also constituted only 25 per cent of the total renal mass and still showed some hydronephrosis after a repair period of four hundred and sixty-five days. The parenchyma of this organ was limited almost entirely to each pole, and grossly this kidney appeared to be more atrophic than any of the others.

If the injured kidney underwent progressive atrophy, we should expect the experiments of the longest "competitive" period to show the greatest degree of atrophy. This is not at all striking in these experiments. The percentages of the renal mass made up by the right kidneys in the experiments of longer duration are somewhat below those in the experiments of short duration, but this difference may well lie within the limits of experimental variation or may be explained by the histologic observations. Some of the experiments showed a rather surprising degree of repair rather than progressive atrophy. This was especially marked in dog A 43, protocol 18, in which after a period of thirteen days of complete ureteral obstruction and a period of repair of one hundred and fifty-four days the relative weights of the kidneys were almost the same.

The studies of the blood urea in these experiments showed no constant or definite changes. In some of the animals a temporary rise was noted after the ligation of the right ureter.

The histologic studies in this group of experiments are especially noteworthy. The left, undisturbed kidneys of these animals served as controls and in most instances were normal. One animal showed changes indicative of chronic, diffuse glomerular nephritis, while several were the seat of a pyelonephritis which was in no case severe. The glomerular tufts were in general plump and hyperemic and often there was a collection of serum precipitate within the capsules.

The right kidneys were hydronephrotic and showed changes that varied with the length of the recovery period. This variation was not absolutely uniform, some animals showing greater repair in shorter periods of time than others. In general, however, the following sequence of changes could be traced throughout the series.

The right kidney of dog A 39, protocol 24, which was obstructed for sixteen days and followed by a repair period of twenty-four days, showed changes only slightly more advanced than those observed in the right kidneys of the dogs of series I. The damage was most severe in the cortex corticis and in the outer zone of the cortex proper while the deeper zone of the cortex appeared normal (fig. 11). There was widespread degeneration of tubular epithelium with tubular atrophy and collapse. The glomeruli appeared to be concentrated in the damaged zone, and although the capsules were of normal size the tufts were exceedingly small. The decrease in the size of the glomerular tufts was not due here to a contraction but to loss of substance, and frequently a mass of necrotic cellular tissue still clung to the remnant of tuft while in other instances the capsular space was partially filled with a structureless granular basophilic mass containing a few fragmented or pyknotic nuclei. Some of the tubules were represented by a small group of degenerated epithelial cells enclosed by a basement membrane while others were lined by young regenerated epithelium containing mitotic figures. With a longer period of repair the fibrous connective tissue reaction to the injury was manifest. The cortex corticis was completely atrophic and persisted only as an irregular thickening of the capsule. There was marked interstitial fibrosis of the outer zone of the cortex proper with radial extensions of the scarring toward the medulla. There was contraction of the fibrosed zones with concentration of glomeruli many of which showed degeneration and fibrosis. Later many of the glomeruli shrank until only a small scar marked their location. The damaged tubules went on either to complete atrophy and disappearance or to epithelial regeneration and restitution. In this stage there was considerable fibrosis of the medulla and in some cases there was a proliferation of the perivascular fibrous connective tissue.

In five of the nine animals in which the period of repair was seventy days or more there was no histologic difference between the right and left kidneys except the reduction in thickness of the right cortex (fig. 10). There was no trace of the destroyed renal tissue in the right kidney of these animals. This observation was of especial interest in view of the fact that there was a definite mass reduction in the majority of the right kidneys and yet there were no signs of the atrophied structures. This would suggest that a glomerulus damaged in the course of hydronephrosis becomes atrophic and can eventually disappear without leaving any trace.

As has already been mentioned, the cortex corticis and outer zone of the cortex proper suffered the greatest damage while the deeper zone of the cortex and the corticomedullary zone appeared unchanged in recent as well as older injuries. This would seem to indicate that the distribution of the damage was associated with the vascular supply of the organ and that the arterial compression incident to the hydronephrosis affected to the greatest degree those glomeruli which were supplied by the terminal branches of the interlobular arteries and that those glomeruli whose blood supply was derived from the larger vessels closer to the arcuate arteries were not damaged by such periods of hydronephrosis as these kidneys experienced (fig. 11). Hinman and Morison² arrived at the same conclusion by arterial injection experiments, and stated that that portion of the kidney receiving the largest and most direct blood supply persisted longest and continued to secrete against the intrapelvic pressure.

SUMMARY AND CONCLUSIONS

Our experiments may be divided into three groups:

Group I: In these experiments the right ureter was completely obstructed for periods varying from thirteen to sixteen days, following which the animals were killed in order that the changes thus produced in the kidneys might be studied. These experiments demonstrated that such a period of ureteral obstruction caused a fairly marked degree of hydronephrosis and renal damage.

Group II: In these experiments the right ureter was completely obstructed for periods varying from eleven to nineteen days, following which the obstruction was relieved and several days later the hypertrophic left kidney was removed. In this way the entire load of renal function was placed on the injured kidney. The period of repair varied between thirty-four and eight hundred and twenty-eight days.

2. Hinman, F., and Morison, D. M.: Experimental Hydronephrosis: Arterial Changes in Progressive Hydronephrosis of Rabbits with Complete Ureteral Obstruction, *Surg. Gynec. Obst.* **42**:209 (Feb.) 1926.

These experiments definitely showed that the injured kidney could undergo a remarkable degree of repair and hypertrophy if the demand were placed on it.

Group III: In these experiments the right ureter was completely obstructed for periods varying from twelve to nineteen days, following which the obstruction was relieved and the injured kidney was allowed to act in "competition" with its undisturbed and hypertrophic mate. This period of "competition" varied between twenty-four and eight hundred and seven days.

This group of experiments bears more directly on the question of renal atrophy of disuse. In no experiment did the injured kidney go on to complete atrophy even though in four of the experiments the period

TABLE 3—*Data on Dogs with Repair of Hydronephrotic Kidney with the Hypertrophic Mate Undisturbed*

Protocol	Duration of Complete Obstruction of Right Ureter, Days	Period of Repair of Right Kidney, Days	Weight of Kidneys, Gm		Percent age of Total Renal Mass	
			Right	Left	Right	Left
13 (Dog A 27)	12	807	40.5	71.5	36	64
14 (Dog A 41)	16	728	16.2	48.7	25	75
15 (Dog A 34)	15	465	15.0	45.0	25	75
16 (Dog A 14)	12	362	14.1	44.2	24	76
17 (Dog A 28)	12	217	31.5	69.2	31	69
18 (Dog A 43)	13	154	38.1	44.2	46	54
19 (Dog A 35)	16	91	11.8	28.7	29	71
20 (Dog A 42)	13	78	28.6	38.3	43	57
21 (Dog A 9)	12	71	16.0	22.0	42	58
22 (Dog A 10)	13	56	9.7	15.4	39	61
23 (Dog A 46)	19	43	19.5	41.0	32	68
24 (Dog A 39)	16	21	17.6	40.4	30	70

of "competition" lasted from one to over two years. Instead of complete atrophy we found that the injured kidneys represented from one-fourth to almost one-half the total renal mass. The pyelographic studies showed that in most instances there was a return to a relatively normally shaped pelvis, although frequently the extrarenal portion of the pelvis and the ureter remained somewhat dilated.

The histologic studies, which were made in all of the experiments, may be summarized as follows:

1. The immediate effects of renal obstruction were manifested first by tubular degeneration and later by glomerular damage. Many of the glomerular tufts underwent partial or complete necrosis with subsequent disappearance of all or part of the renal unit.

2. Those kidneys which after a period of total ureteral obstruction ranging from twelve to nineteen days were allowed by relief of the obstruction to work in "competition" with their hypertrophic and undisturbed mates showed no evidence of progressive atrophy. The injured

renal elements either recovered or completely disappeared. In those experiments in which the period of repair was seventy days or more, histologic differences between injured and noninjured kidneys were not seen in five of nine animals. The other four showed varying stages of recovery.

3. Those kidneys which after a period of total ureteral obstruction ranging from eleven to nineteen days were forced to carry the entire functional load recovered rapidly, and no trace of the damaged renal units could be seen after a period of repair of forty-two days or more.

Our experiments did not demonstrate any renal atrophy of disuse and, in fact, strongly suggest that such atrophy does not occur.

In view of the experimental data presented, the theory of renal counterbalance need not be seriously considered in deciding the surgical treatment for certain renal lesions.

THE DELBET APPARATUS AND THE END-RESULTS*

EDWARD T. CROSSAN, M.D.

PHILADELPHIA

The ability to apply knowledge is a valuable possession. By this faculty, Delbet has applied the common knowledge of surface anatomy to the development of a new treatment for fractures of the leg and of the ankle. He has utilized the prominence of the malleoli and the projections of the internal tuberosity of the tibia and of the head of the fibula as points d'appui for a splint which will fix the fracture without immobilizing the knee or ankle. With good function as the goal of the treatment, Professor Delbet could not have overlooked a method of securing good reduction and solid union.

Good reduction easily secured, consolidation of the fracture stimulated, good function restored in a comparatively painless manner and the disability reduced to a minimum period without the aid of physiotherapy are the benefits I hope to demonstrate by describing again the Delbet apparatus and by reporting the end-results with this method of treatment.

DELBET APPARATUS

Materials.—1. A thin, flat board is used, which is covered on one side by zinc and to one end of which is attached a pulley at such a height that traction over it will be directly in the long axis of the bones of the leg (fig. 1, A). The pulley is movable laterally so that any lateral deformity can be corrected without disturbing the fracture.

2. A scultetus, or many-tailed bandage, made long enough to extend from the heel to the knee is used; the loose ends on each side are wrapped in a narrow piece of cardboard for convenience in handling.

3. Four splint forms made of crinoline are needed. Figure 2 shows in detail the measurements and the shapes of the forms. The forms are basted down the middle (the dotted line on the form in figure 2). Plaster of paris is incorporated in each layer of the crinoline as in the preparation of a plaster bandage,¹ and the forms, with their meshes filled with the dry powder, are wrapped in waxed paper and stored until occasion for use arises.

METHOD

Preliminary Procedures.—The board, zinc side up, is placed beneath the fractured limb. To prevent rotation of the fragments, the toes of the injured limb are held by an assistant. The leg is washed with soap and water, rinsed with

* Submitted for publication, March 16, 1929.

* From the clinic of Dr. A. P. C. Ashhurst, Episcopal Hospital.

1. This method of the preparation of the forms differs from the directions laid down by Delbet, and the cause for the modification will be noted later in the paper.

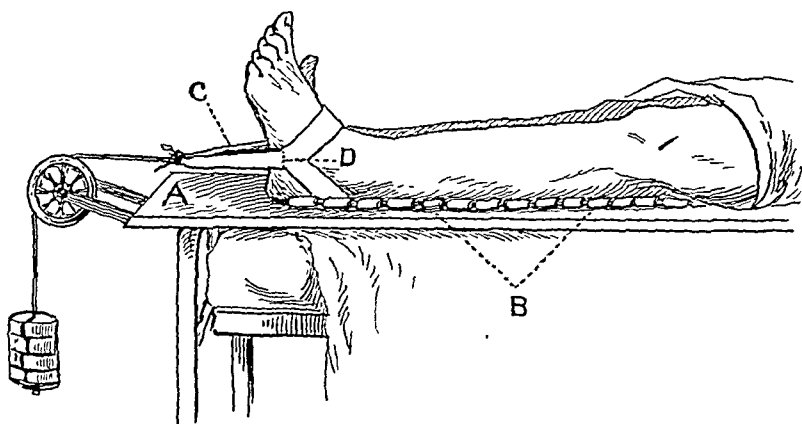


Fig. 1.—Method of applying traction: *A*, board; *B*, scultetus; *C*, traction loop, and *D*, overlapping of the flannel piece for the traction loop.

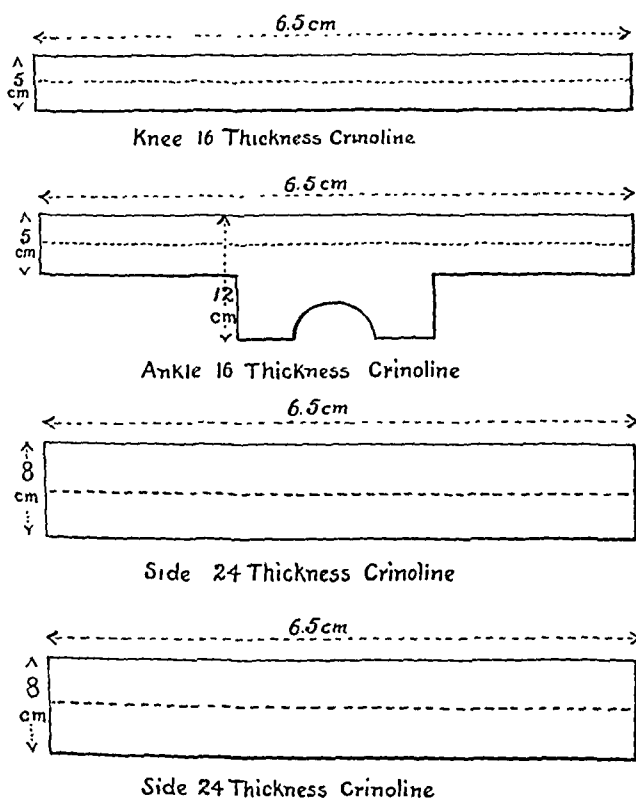


Fig. 2.—Measurements and shapes of splint forms.

alcohol and powdered; shaving is not necessary. Next, the scultetus is gently worked into position between the leg and the board (fig. 1, *B*).

Reduction.—A stirrup is made by using two strips of narrow flannel bandage (3 by 45 cm.). One strip is placed beneath the tendo achillis and above the heel. The second strip is passed over the dorsum of the foot, just distal to the ankle joint. The strips are crossed on each side below and posterior to the malleolus, and at the point of overlapping they are stitched together (fig. 1, *D*). The four loose ends (two from each strip) are carried to a suitable distance below the sole of the foot, and a loop is made by tying or stitching the ends together. To the loop (fig. 1, *C*) is attached the rope which will carry the weights.

The weights are added gradually so as to prevent spasm of the muscles. No manipulations (attempts to push fragments into place) are employed. If the preceding instructions are observed there is little pain, and no anesthetic is required. The pain ceases as soon as the weight begins to act. Repeated measurements are made to determine reduction. When reduction has been obtained, the splint is applied without disturbing the traction apparatus.

Application of the Splint.—Step 1: The ankle and the knee forms (fig. 2) are immersed in water, and when they have been saturated, they are spread out on a table and plaster of paris powder is sprinkled over both sides of each splint.

Step 2: The ankle form is placed in position by (*a*) passing one of the narrow ends through the gap which exists between the heel and the point where the calf of the leg comes into contact with the board; (*b*) gentle traction pulls through one of the wings (the area 12 cm. wide in figure 2); (*c*) the notch in the form is placed above the os calcis; (*d*) the wings are placed opposite the malleoli and the lower end carried down to within 1 cm. of the sole, and (*e*) the narrow ends and the entire form of crinoline are spread out on the board.

Step 3: The knee form (fig. 2) is passed under the knee, across the popliteal space. By seesaw motions it is moved downward to a position below the tibial tubercle, and the ends are spread out on the board.

Step 4: During steps 2 and 3, an assistant soaks the side forms by the method described in step 1. These forms are applied to the sides of the leg from the knee to within 1 cm. of the sole and then turned upward on themselves so as to provide an extra support for the subastragalar joint and the ankle joint.

Step 5: The spread out ends of the ankle piece are carried obliquely upward across the front of the leg and onto the opposite side splint. The ends must be crossed at or slightly above the point where the tendon of the tibialis anticus becomes subcutaneous. This ankle piece thus holds the lower ends of the side splints against the malleoli and the sides of the leg.

Step 6: The ends of the knee piece are carried across the front of the leg over the tibial tubercle, and serve to hold the upper ends of the side splints against the leg. Figure 3, *A* shows the splint applied and the manner of crossing of the extremities of the ankle and knee forms.

Step 7: The ends of the scultetus (fig. 1, *B*) are unwrapped from their cardboard and the strips are crossed obliquely from below upward.

Step 8: When the plaster has set firmly enough to give a clear sound on tapping with the fingers, the weights are removed and the stirrup is cut on the dorsum of the foot, and is removed entirely. The continued traction prevents displacement of the fragments during the application and setting of the splint. Traction should not be continued longer than twenty-five minutes, because of the danger of sloughs over the dorsum of the foot or on the heel.



Fig. 3.—*A*, anterior aspect of splint applied. *B*, posterior aspect of same splint. *C*, lateral aspect of same splint. *D*, the flexion of the knee is not impeded by the splint.

With the aid of two assistants, the surgeon usually can apply the Delbet apparatus in from ten to twelve minutes, including the time allowed for the weight traction to overcome the deformity. Figure 3 shows the splint applied.

PRECAUTIONS

The precautions to be observed in applying the splint are as follows:

1. No attempts at manual reduction should be made during the process.
2. The knee pieces should not be carried too high because full flexion of the knee would be prevented.
3. The ankle pieces should be crossed above the point where the *tibialis anticus* becomes subcutaneous. If they are crossed below this point, a pressure sore will result from rubbing of the tendon against the edge of the splint when the foot is dorsiflexed.
4. The side pieces should not extend as far down as the sole.
5. Traction should not be too prolonged.

TREATMENT AFTER APPLICATION

The patient is returned to bed, the leg is elevated high (six pillows) and is surrounded by ice bags. By the strict observance of these regulations swelling can be prevented. If swelling should occur, a vicious cycle would be established resulting in troublesome ulcers.

The day following the application, the scultetus is removed, and on the same day active motions of the knee and ankle are started. Most patients are able to raise the limb from the pillows and kick it around actively the morning after the splint has been applied. In a week or ten days, the patient is removed from bed and is advised to bear weight on the injured limb with the support of crutches; at each step the patient bends the knee, bends the ankle and comes up on the toes. During the third or fourth week the crutches are discarded for a cane, and at about this time some patients, particularly children, walk without any support. The splint is removed in six weeks, and the patient returns to work as soon as confidence in the injured limb is regained. Many patients will not use the injured limb as advised, unless the surgeon takes the trouble to walk with them at first to instruct them. When they have learned, they will walk, gladly.

SUMMARY

The fracture, as all fractures should be, is reduced immediately. The reduction is by gradual traction, and the fracture is immobilized by a splint which does not interfere with motions of the knee or ankle (fig. 3). Walking encourages consolidation, because the medullary

callus is approximated in the weight-bearing.² Displacement of the fragments is prevented by the close application of the side splints to the bony prominence of the leg.

END-RESULTS

In the compilation of the accompanying tables, I have adhered strictly to the definitions of the Fracture Committee of the American Surgical Association:

1. The anatomic result means the position of the fragments at the time of union.

2. A bad anatomic result is one in which there is gross deformity, or shortening of more than 2 cm.

3. Moderate anatomy is a variant of the foregoing results.

4. Good anatomy indicates that there is no appreciable deformity.

5. If there are no symptoms, the result is classed as good function.

6. Pain in damp weather or swelling, limp or lessened endurance classify the result as moderate function.

7. Bad function means that the earning capacity was reduced, that a change of occupation was necessary or that there was a serious interference with the functions of the joints.

The splint was first used in the Episcopal Hospital during October, 1922. In this study are included all of the patients with fractures of the leg and of the ankle admitted to Dr. Ashhurst's service between October, 1922, and October, 1927, excluding those of 1928, because in some of the cases, the results are too recent to be classed as end-results.

During the five year period ninety-nine patients were admitted. In two of the patients the fractured leg was the less severe injury, and death occurred a few hours after admission. A third patient had an amputation of the leg for uncontrollable hemorrhage from a compound fracture. A fourth patient, not treated by the Delbet method, died from fat embolism soon after the removal of a Steinmann pin.

Seventeen of the ninety-five cases of fractures were unsuitable for the Delbet method, and twelve other patients were not treated by it; the site of the fracture and the variety of the fracture in these twenty-nine cases are shown in tables 1 and 2. At this point it should be noted that the unsuitable cases are (1) fractures above the middle third of the leg because the immobilization for such fractures should include the knee, and (2) severe compound fractures or fractures complicated by severe lacerations or abrasions, because the splint interferes with dressings; however, in these cases the splint can be used when the wounds are healed.

2. J. F. Cowan recently showed that the separation of the medullary callus is probably the cause for nonunion (*Ann. Surg.* 88:749, 1928).

Sixty-six patients, or 87 per cent of the suitable cases, were treated by the Delbet method, and if the twelve patients noted in table 2 had had this treatment, the results to be reported subsequently would have been more impressive. Fifty-three of the sixty-six patients treated by the Delbet method have been traced: one patient died of carcinoma of the stomach soon after discharge from the hospital and is excluded from the study.

TABLE 1.—*Unsuitable Cases*

	Cases
Fracture tuberosity tibia.....	5
Fracture of spine of the tibia.....	1
Severe compound fractures.....	4
Bad skin conditions.....	4
Children under 3 years.....	2
Fracture with pneumonia.....	1
Total	17

TABLE 2.—*Not Treated by Delbet Apparatus*

	Cases
Incomplete fractures.....	7
Children with simple fractures.....	4
Compound fracture (small wound).....	1
Total	12

TABLE 3.—*Diagnosis in Untraced Cases**

	Cases
Tibia and fibula. shaft.....	5
Shaft o.....	4
Fibula,.....	1
Ankle fracture (A2).....	2
Bimalleolar fracture.....	1
Total	13

* Ten were over 15 years of age, three were under 15 years.

In table 3, the site and the variety of the fractures of the patients not traced are shown. Table 4 shows the variety of fractures, the site and the age incidence of the traced cases. By comparing tables 3 and 4, it will be seen that the fractures of patients not traced were not more severe than those of patients who were followed; also, the age incidence in the two groups is nearly the same. One of the untraced patients, a fat woman, who could not be induced to walk, had delayed union on discharge (refused operation), and she probably has a bad result.

In 1921, Dr. Ashhurst and I reported before the American Surgical Association³ the end-results of a series of 100 cases of fracture of the leg and ankle in which the patients were treated in Dr. Ashhurst's clinic at the Episcopal Hospital, and in table 5 I have abstracted those results to serve as a standard for comparison with the present report. There are few compound fractures in the present series; therefore, table 5 does not include the results of any compound fractures.

TABLE 4.—*Diagnosis in Fifty-Two Traced Cases*

	Patients Under 15 Years	Patients Over 15 Years
Shaft of tibia, simple	7	2
Shaft of tibia, compound	1	0
Shaft of fibula, simple	1	2
Shaft of tibia and fibula, simple	5	11
Shaft of tibia and fibula, compound	1	0
Fibula, external malleolus (A1)	0	1
Shaft of tibia, incomplete	0	6
Tibia and fibula at ankle (A2, A3, Pott's)	0	14
Tibia and fibula at ankle, compound	0	1
Total	15	37
		52 patients

TABLE 5.—*Results Reported by Ashhurst and Crossan in 1921**

	Good, per Cent	Moderate, per Cent	Bad, per Cent
Anatomic	82	16	2
Functional	75	22	3

* The period of disability in seventy four simple fractures of the leg and ankle was four months

TABLE 6.—*End-Results in Patients Treated with the Delbet Apparatus*

	Anatomic		Functional		
		Good	Moderate	Bad	
Good	43 (83 per cent)	40 (93 per cent)	2 (5 per cent)	1 (2 per cent)	
Moderate	7 (13 per cent)	4 (57 per cent)	3 (43 per cent)	0 ()	
Bad	2 (4 per cent)	0 ()	1 (50 per cent)	1 (50 per cent)	
	52	44 (85 per cent)	6 (11 per cent)	2 (4 per cent)	

In table 6 are recorded the results of the fifty-two traced cases. The results do not represent the work of one surgeon, nor of a specialized group; a large number of the splints have been applied by many different resident physicians and interns.

There has not been any change in the good anatomic results of the series in table 6 over the series in table 5, and this observation was to be expected because good reduction in most cases can be obtained by one means or another—skeletal traction, open reduction, etc. In this

³ Ashhurst, A. P. C., and Crossan, E. T.: Prognosis and Treatment of Fractures of Leg and Ankle: End-Results in 100 Patients, Arch Surg. 7:601 (Nov.) 1923

series, however, reduction was secured in all of the cases by the closed method and without any skeletal traction, whereas, in nineteen of eighty-five cases of simple fractures, in the report of 1921, reduction was obtained by the following methods: six platings, six screw fixations at the ankle, four cases of skeletal traction (Steinmann) and two tenotomies of the tendo achillis. The present report seems to prove that reduction of a fractured leg is more easily secured by the Delbet method of traction.

Good functional results in this series (table 6) were obtained in forty-four cases, or 85 per cent, an increase of 10 per cent over those shown in table 5. In the report of 1921, 85 per cent of the patients who had good anatomy had good function as compared to 93 per cent with good function in patients with good anatomy treated with the

TABLE 7.—*Influence of Age in Cases in Which Delbet Apparatus Was Used **

Under 15 Years				
	Anatomic	Functional		
		Good	Moderate	Bad
Good	14 (93 per cent)	14 (100 per cent)	(.....)	(.....)
Moderate ..	1 (7 per cent)	1 (100 per cent)	(.....)	(.....)
Bad	0 (.....)	0 (.....)	0 (.....)	0 (.....)
	15 (100 per cent)	15 (100 per cent)	0 (.....)	0 (.....)
Over 15 Years				
	Anatomic	Functional		
		Good	Moderate	Bad
Good	29 (79 per cent)	26 (89 per cent)	2 (7 per cent)	1 (3 per cent)
Moderate ...	6 (16 per cent)	3 (50 per cent)	3 (50 per cent)	0 (.....)
Bad	2 (5 per cent)	0 (.....)	1 (50 per cent)	1 (50 per cent)
	37 (100 per cent)	29 (79 per cent)	6 (16 per cent)	2 (5 per cent)

* In a series of eighty adults reported by Ashhurst and Crossan in 1921, anatomic results were the same, functional results were good, 65 per cent; moderate, 32 per cent, and bad, 2 per cent.

Delbet splint (table 6). It is possible that a higher percentage of good functional results in an accurately reduced fracture will be obtained by the latter method, because there are no fibrous contractures of the muscles nor of the ligaments; however, I believe that the improvements in the second report can be attributed to the absence of any operative procedure in this group. Experiences and observations have convinced me that there is a higher percentage of good functional results in fractures reduced by the closed method than in those reduced by operative procedures. In the series of operative reductions reported in 1921 (included in the results of table 5), only 73 per cent of the good reductions resulted in good function, which is 12 per cent less than the results in the group here reported (table 6). Good reduction easily secured will give the best functional results.

The termination of disability denotes the restoration of good function in most cases of fractures; therefore, the period of disability

should be a fairly accurate index of the efficacy of the method of treatment. In addition to good anatomy, good function depends on the restoration of motion in the joints bordering the fracture, on the reeducation of the muscle groups and on the establishment of an efficient venous return. Immobilization of a fracture of the leg or of the ankle by a circular cast or by a molded plaster (Stimson) splint is always followed by stiffness of the ankle, the knee or both joints, and by swelling of the leg. With the Delbet splint there is no artificial support to the venous column, there is no interference with the motions of the points (except the astragalocalcanean), and there is no hindrance to muscle action and muscle pumping on the veins; therefore, the stiff-



Fig. 4.—Swelling of left lower extremity after the removal of a circular cast.

ness mentioned, or the swelling as shown in figure 4, is rarely seen. Furthermore, with the Delbet splint, confidence in the injured limb returns at an early date because of the weight-bearing during consolidation. With good reduction, immobilization of a fractured leg or ankle by the Delbet splint should reduce the disability to a minimum period.

In a series of thirty-seven adults, the disability was shown in thirty-five.⁴ The average disability of this group was three and one-half months, a reduction of one-half month, or 25 per cent, over the period

4. One of the two patients in whose cases the period of disability is unknown had an incomplete fracture of the tibia; on account of litigation, he refused to tell the period of disability. The other patient, with a fracture of the shafts of the tibia and fibula, returned to Italy.

noted in the footnote of table 5, and a reduction of nine tenths of a month over a series reported by the American Surgical Association in 1921. In only one of thirty-five cases were baking and massage used, which means that there has been a great saving of time and money. There has been an increase of 2 per cent in the bad anatomic and of 1 per cent in the bad functional results; however, the percentages in both groups are less than those reported by the American Surgical Association. The 4 per cent with bad anatomy and the 3 per cent with bad function represent three patients; one (C. G.) had bad anatomy and bad function, a second (H. B.) had bad anatomy and moderate function, and the third (R. R.) had good anatomy and bad function. Two of the bad results are directly traceable to failure of the splints to harden.

During the first eighteen months that the splint was used, soft splints were a frequent occurrence. During that period the forms were pre-

TABLE 8—Results Since January, 1924 (Twenty-Nine Patients Over 15 Years, Twelve Under 15 Years) *

	Anatomic	Functional		
		Good	Moderate	Bad
Good	35 (85 per cent)	33 (91 per cent)	1 (3 per cent)	1 (3 per cent)
Moderate	6 (15 per cent)	3 (50 per cent)	3 (50 per cent)	0 ()
Bad	0 ()	0 ()	0 ()	0 ()
	41 (100 per cent)	36 (90 per cent)	4 (8 per cent)	1 (2 per cent)

* The period of disability of twenty nine adults was two and eighty six hundredths months (two and seventy six hundredths months for fractures of the leg and two and ninety four hundredths for fractures of the ankle)

pared by immersion in a creamy mixture made by adding plaster of paris to water, the method prescribed by Professor Delbet.

Early in 1924, at the suggestion of Dr. Winter, then a resident physician, Dr. Ashhurst adopted the modification noted previously in the discussion of splint forms under the heading materials. Since January, 1924, there has been only one soft splint,⁵ and in this instance the plaster cream method was used.

In table 8, I have compiled the results since January, 1924. In this group there have not been any bad anatomic results and only one bad functional result. The good anatomic and the good functional results have not materially changed. The average period of disability in this group of twenty-nine adults, however, was two and nine-tenths months, a reduction of one and one-tenth months over the series of 1921. The period of disability in this group, I believe, is about the minimum that can be obtained by any method.

5 A soft splint replaced by Stimson was followed by peroneal palsy (R R, case 2 under bad function)

In this series of fifty-two patients, there were twelve who did not obtain both good anatomy and good function. The deformities and the disabilities of the twelve patients are as follows:

Moderate Anatomy (Seven Cases).—CASE 1.—A child, aged 9 years, with a fracture of the shaft of the tibia, regained perfect function but had a slight bowing at the site of fracture.

CASE 2.—R. W., a man, aged 43, had had a fracture of the lower ends of the tibia and fibula (A3⁶) for which he had been treated in another institution for three weeks. Final examination showed bowing at the site of the tibial fracture and a shortening of 0.5 cm.; joint motions were normal, and he was free from symptoms. He returned to the same work in three months, and his wages were the same. The result was classed as good function.

CASE 3.—W. J., a man, aged 54, as a result of fractures of the lower third of the tibia and fibula, had a moderate fulness over the tibial fragment due to overriding. Shortening could not be measured, because the other leg was markedly deformed as a result of a fracture sustained eighteen years before. He returned to the same work, earned the same wages and was free from symptoms. The result was classed as good function.

CASE 4.—N. D., a woman, aged 54, had a fracture of the lower end of the tibia and of the external malleolus. Relatives reported that she had pain for two years and was disabled for one year. The final x-ray picture at the hospital showed slight posterior displacement of the lower fibular fragment. The result was classed as moderate function.

CASE 5.—S. P., a man, aged 42, had a fracture of the lower ends of the tibia and fibula (A3). At the final examination a convexity was noted over the tibial fracture without shortening. In three months he returned to the same work and earned the same wages. There was perfect function of all the joints, but because he limped slightly, the result was classed as moderate function.

CASE 6.—A. D., aged 52, had a fracture of the lower ends of the tibia and fibula (A3). On account of slight valgus the function was classed as moderate anatomy. The patient returned to work in ten weeks, but the leg swelled at the end of the day, on account of which the result was considered moderate function.

CASE 7.—J. N., aged 50, had a fracture of the middle third shafts of the tibia and fibula. The function was considered a moderate anatomic result because of convexity over the tibial fracture and a shortening of 0.5 cm. The patient returned to the same work in fifteen weeks, earned the same wages and had no symptoms, and therefore was considered as having good function.

Moderate Function (Six Cases).—CASE 1.—N. D., case 4 under moderate anatomy.

CASE 2.—S. P., case 5 under moderate anatomy.

CASE 3.—A. D., case 6 under moderate anatomy.

CASE 4.—E. C., had a Pott's or B2 fracture with good anatomy, but dorsiflexion of the ankle was limited to 90 degrees.

6. In the case reports, A3 indicates a fracture of the lower end of the fibula plus a fracture of the whole lower end of the tibia. B2 represents a fracture of the internal malleolus plus a fracture of the fibula. A1 indicates a fracture of the lower end of the fibula only. (Ashhurst, A. P. C., and Bromer, R. S.: Classification and Mechanism of Fractures of the Leg Bones Involving the Ankle, Arch. Surg. 4:120 [Jan.] 1922.)

CASE 5.—L. B. had a bimalleolar fracture with excellent anatomy, but had a rigid flatfoot. The patient returned to the same work in fifteen weeks.

CASE 6.—H. B., to be noted under bad anatomy.

Bad Anatomy (Two Cases).—CASE 1.—G. C., aged 32, had fractures of the lower end of the tibia and external malleolus (B2). Two Delbet splints failed to harden. Final examination three years after injury showed marked valgus. The patient had constant pain, was disabled nine months, and the earning capacity was "considerably reduced." The result also was classed under bad function.

CASE 2.—H. B., aged 54, had a fracture of the shafts of the tibia and fibula. Three Delbet splints failed to harden. The final result was a marked prominence over the tibial fracture, a shortening of the leg of 1 cm. and a limitation of flexion of the knee at 90 degrees. The patient returned to the same work in nine months and earned the same wages. The result was classed previously under moderate function.

Bad Function (Two Cases).—CASE 1.—G. C., case 1 under bad anatomy.

CASE 2.—R. R., a woman, aged 35, had an oblique fracture of the lower end of the fibula (A1). Two Delbet splints failed to harden. Stimson splints were applied and on removal a peroneal palsy was noted, which has persisted for three years.

CONCLUSIONS

Though the study of the entire five year period shows an improvement in functional results and a reduction of the period of disability, I believe that the results since January, 1924, are more representative of what can be accomplished by the Delbet apparatus. With this method, the return of function and the period of disability are dependent on the patient's persistence in the use of the injured member. Walking on the injured leg with the splint does not cause pain; it is timidity which must be overcome. Reduction of the fracture is easily secured, and there is nothing complicated about the application of the immobilizing apparatus. There are, of course, certain precautions to observe.

TRAUMA TO CENTRAL NERVOUS SYSTEM

ITS EFFECTS ON CARDIAC OUTPUT AND BLOOD PRESSURE AN EXPERIMENTAL STUDY *

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Operations on the central nervous system are frequently accompanied by a marked diminution in the blood pressure. This decline in pressure, however, is not of as grave concern as a like drop in blood pressure during an abdominal operation. The pressure may reach a low level during an operation on the central nervous system, but if the operative procedure is stopped immediately, the pressure will usually rise without any artificial aid. In a report from the surgical clinic of Dr. Harvey Cushing, Bird¹ stated, "During operations for intracranial tumors, patients have been observed who, though their blood pressure remained too low to be recorded for from thirty minutes to three hours, recovered after spontaneously 'picking up' or following transfusion, without detectable injury to nervous tissue or other permanent ill effect." Most of these patients had lost a moderate amount of blood.

The use of the word "shock" is intentionally avoided in the title of this paper because the opinion has been expressed by several competent investigators that the syndrome usually entitled "shock" cannot be produced by injury to the central nervous system. Vincent,² from his experience during the war, stated that he never saw a case of shock which resulted from an injury which was limited to the central or peripheral nervous system. Mann³ said that it was impossible to produce shock in a dog without opening the abdomen, without inducing hemorrhage or without traumatization of the medullary centers. He stated further that an animal with a very low blood pressure owing to section of the spinal cord in the lower cervical or upper thoracic region is not in a condition of surgical shock, because upon withdrawal of the anesthetic the animal will regain consciousness and respond to stimuli applied around the head. In Mann's experiments, the fall of blood

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1. Bird, C. E.: Transfusions in Acute Loss of Blood, *Arch. Surg.* **18**:1646 (April) 1929.

2. Vincent, C.: Contribution à l'étude de l'état de shock primitif chez les blessés de guerre, *Compt. rend. Soc. de biol.* **81**:887, 1918.

3. Mann, F. C.: The Peripheral Origin of Surgical Shock, *Bull. Johns Hopkins Hosp.* **25**:207, 1914.

pressure following section of the cord was no greater than the decrease which immediately followed section of the abdomen and exposure of the viscera. He was unable to produce shock in anesthetized animals after hours of traumatization of the great nerve trunks. Guthrie⁴ and Wiggers⁵ were able to produce what they considered as shock, the former by prolonged stimulation of the brachial plexus, the latter by stimulation of sensory nerves or by crushing the testes. Shock was not produced in all animals in which these methods were used. Guthrie stated, "Susceptibility varied greatly in different dogs. Some animals readily succumbed to brachial nerve stimulation alone; others only when nerve stimulation was combined with opening the abdominal cavity and visceral manipulation; while others were highly resistant under both methods."

The purpose in this paper is to record the changes observed in body temperature, pulse rate, maximum and minimum arterial blood pressures, cardiac output and consumption of oxygen produced by trauma to the cerebrum, the cervical cord and the thoracic cord.

METHOD

Dogs were used in all of the experiments. The anesthetics which were employed in different instances were morphine, chloralose and barbital. The anesthesia produced by morphine was not sufficiently profound during the stage of the operation and it was supplemented by light ether anesthesia. In most instances, the following procedure was carried out: After the animals had been narcotized for varying intervals of time, control determinations of the various factors were made. An operation was then performed which had for its object the exposure of the dura overlying the area of the central nervous system which was to be traumatized. The studies were repeated at this stage. The dura was then opened without trauma to the brain or cord, and the third series of studies were performed. The brain or cord area was then traumatized with the finger, and varying numbers of studies on the various functions were performed. The arterial blood pressure readings were obtained by placing in the femoral artery a cannula which was connected with a mercury manometer; maximum and minimum valves were used in most instances. A Benedict spirometer was employed in determining the consumption of oxygen. The connection between the animal and the spirometer was made either by the use of a tracheal cannula or by a specially constructed rubber mask which made an airtight closure over the animal's mouth. Samples of blood were withdrawn under oil and placed under oil in order to avoid contact with air. Arterial blood was obtained from the femoral artery and mixed venous blood from the right side of the heart. The analyses of the blood gases were performed with the van Slyke-Neill manometric apparatus. The output of the heart was computed by the Fick principle:

$$\frac{\text{Oxygen consumption per minute}}{\text{Arterial oxygen content minus venous oxygen content}} = \frac{\text{Number of cubic centimeters of blood flowing through the lungs per minute}}{\text{Number of cubic centimeters of blood flowing through the lungs per minute}}$$

4. Guthrie, C. C.: *Experimental Shock*, J. A. M. A. **69**:1394 (Oct. 27) 1917.

5. Wiggers, C. J.: *Shock and Circulatory Failure Following Trauma*, Am. J. Physiol. **46**:314, 1918.

RESULTS

The effects of the operation, of the opening of the dura and of the trauma were not the same in all experiments. The observations on the effects of injury to the cerebrum, the cervical cord and the thoracic cord will be considered separately.

Trauma to the Cerebrum.—Ten experiments were performed in this group. Five of the animals were anesthetized by morphine, four by chloralose and one by ether. Ether anesthesia was unsatisfactory because of the enormous change which it caused in the output of the heart. The pulse rate increased in all experiments. The body temperature showed practically no change throughout the observations in the six experiments in which it was determined. There was little alteration in the oxygen content of the arterial blood. Usually the oxygen content of the mixed venous blood showed a progressive fall, and hence there was usually an increase in the arteriovenous difference.

There was little alteration in the consumption of oxygen in most of the experiments. On comparing the consumption of oxygen during the period shortly following the operative exposure of the dura with that of the control period, it was found to be the same in eight of ten instances, and to be slightly elevated in the remaining two. Immediately after opening the dura, the consumption of oxygen was practically the same as that in the control period in seven of ten instances and was slightly elevated in three. Varying degrees of trauma had no effect on the consumption of oxygen in six of ten instances; there was an increase in one experiment and a fall in three.

The exposure of the dura was associated with no change in the cardiac output in two of the ten experiments; there was an increase in the cardiac output in two instances and a decrease in six. When the dura was opened, the cardiac output remained the same as that for the control period in two experiments; it was elevated in one and decreased in seven. The fall usually consisted, in the main, of that which had been caused by the operative exposure of the dura, and the opening of the dura itself seemed to have little effect. Trauma to a cerebral hemisphere was associated with a fall in the output of the heart in seven of the experiments, with first a rise followed by a fall in two cases and by a sustained rise in one. A great deal of trauma was necessary in most instances to alter the cardiac output.

Protocol 1: Feb. 8, 1929, weight of dog, 10 Kg.; 9 a. m., 0.081 Gm. morphine; 10:40 and 11:35 a. m., control determinations; from 11:55 to 12:15, under ether anesthesia, dura of right cerebrum exposed, not opened; 12:30, 0.049 Gm. morphine; 1 p. m., forty-five minutes after operation, determinations; 1:30, dura opened with no ether; 1:55, twenty-five minutes after opening dura, determinations; 2:20, brain traumatized with finger for about five minutes; 2:45, twenty-five minutes after traumatizing brain, determinations; 3:15, fifty-five minutes after

traumatizing brain, determinations, 3 40, eighty minutes after trauma, determinations, 3.50, slight additional trauma; 4.05, fifteen minutes after additional trauma, determinations.

Exposure of the dura was associated with a decrease in the maximum blood pressure in six of the ten experiments and with no alteration in four. In three of the experiments there was a slight fall in the maximum pressure on opening the dura, but there was no appreciable alteration in the other instances. Trauma to the brain produced a fall in pressure in all experiments, but in several instances it had to be continued until the brain was badly macerated. Changes in blood pressure could be produced more readily by pressure at the base of the cerebral hemi-

TABLE 1—*Result of Trauma to the Cerebrum, on Cardiac Output and Blood Pressure*

Time	Pulse Rate, per Minute	Temperature °	Arterial Oxygen, Volumes per 100 Cc	Venous Oxygen, Volumes per 100 Cc	Arteriovenous Difference, Volumes per 100 Cc.	Arterial Blood Pressure		Oxygen Consumption, Cubic Centimeters per Minute	Cardiac Output per Minute Cc
						Maximum	Minimum		
10 40 control	48		21.84	15.00	6.84	168	94	96.00	1467
11 30 control	54	98	22.92	16.08	6.84	170	78	84.34	1234
1 p m (45 min after exposure of dura)	60	.	20.64	16.20	4.44	176	91	85.66	1929
1.35 (25 min after opening dura)	58		20.76	14.28	6.48	159	79	110.70	1708
2 45 (25 min after traumatizing brain)	124	98	19.80	18.20	6.60	132	74	89.61	1337
3.15 (50 min after brain trauma)	140		19.74	11.04	8.70	118	82	84.34	970
3 40 (80 min after trauma)	175		19.74	9.48	10.34	98	70	73.80	714
4 05 (15 min after additional trauma)	108	98	19.08	8.88	10.20	86	57	68.53	672

spheres. It was noted that pressure in some areas at the base which were not accurately localized was associated with marked temporary elevations in the blood pressure.

The minimum blood pressure was not affected by the operative exposure of the dura in four of the experiments; in three instances it was slightly elevated, and in three it fell. After opening of the dura, the pressure fell slightly in five experiments and rose slightly in three. After traumatization of the brain, the minimum pressure fell in nine of the ten experiments.

The decline in maximum blood pressure, minimum blood pressure and cardiac output usually occurred simultaneously and to approximately the same degree. Increase in pulse rate usually preceded a decrease in the functions just mentioned.

Protocols and tables 1 and 2 give the data on individual experiments.

PROTOCOL 2: March 5, 1929, weight of dog, 10 Kg.; 9:30 a. m., 0.098 Gm. morphine; 11:20, control; from 12:05 to 12:12, left cerebrum exposed, with little loss of blood; slight ether anesthesia employed; dura not opened; 1:55, 103 minutes after operation, determinations; 2:50, three minutes after opening dura, determinations; from 3:16 to 3:19, brain traumatized; 3:21, two minutes after trauma, determinations; 3:35, blood pressure had fallen a great deal; no further trauma; determinations.

Trauma to the Cervical Cord.—Six experiments of this type were performed. Morphine was used as the anesthetic in most instances. It was found in several experiments that the dura could be exposed and opened without causing any alteration in the cardiac output or in the blood pressure. Trauma to the cervical cord produced a cessation of respirations in all experiments except one. The respiratory movements

TABLE 2.—*Results of Trauma to the Cerebrum, on Cardiac Output and Blood Pressure*

Time	Pulse Rate per Minute	Temperature °F.	Arterial Oxygen, Volumes per 100 Cc.	Venous Oxygen Volumes per 100 Cc.	Arteriovenous Difference, Volumes per 100 Cc.	Arterial Blood Pressure		Oxygen Consumption, Cubic Centimeters per Minute	Cardiac Output per Minute, Cc.
						Maximum	Minimum		
11:20 a. m., control.....	60	19.20	13.68	6.12	140	52	85.33	1394
1:55 (103 minutes after exposure of dura).....	160	100.8	19.32	10.44	8.88	110	54	88.79	1000
2:50 (3 minutes after opening dura)	164	100.8	18.72	8.88	9.84	104	58	80.72	820
3:21 (2 minutes after trauma to brain)	200	100.9	19.20	6.60	13.20	98	58	80.72	612
3:35 (16 minutes after trauma to brain).....	200	101.0	18.60	3.00	15.60	37	20	53.04	340

would first become slow and then shortly stop entirely. An effort toward respiration, however, was being made by the accessory respiratory muscles, as was evidenced by movements of some of the muscles of the neck and face. The pulse became very slow and remained strong for a long period, during which tracheal insufflation was instituted.

In the one experiment in which trauma to the cervical cord did not produce immediate death, several series of determinations were made. The cardiac output was not determined before the dura was exposed, but this procedure caused no alteration in the arterial pressure. The cardiac output, the maximum blood pressure, the minimum blood pressure and the mean blood pressure declined together. The decrease in cardiac output was associated with practically no alteration in the oxygen consumption and with an increase in the arteriovenous difference in oxygen content. The results of this experiment are given in table 3.

PROTOCOL 3: Jan. 15, 1929, weight of dog, 9 Kg.; 11 a. m., 0.098 Gm. morphine; 11:30, blood pressure 120 systolic, 80 diastolic; from 11:45 to 12:15, spinal cord

in midcervical region exposed for about 3 cm., with a small loss of blood; ether anesthesia; dura not opened; 1:45, ninety minutes after exposure of dura, determinations; 2:15, dura opened; cord not traumatized; 2:20, five minutes after opening dura, determinations; 2:40, twenty-five minutes after opening dura, determinations; from 3:14 to 3:18, cord traumatized with finger; 3:26, eight minutes after trauma ended, determinations; 3:52, thirty-four minutes after trauma to cord, determinations.

Trauma to the Thoracic Cord.—Three experiments of this type were performed. Morphine was used as a narcotic. Usually the dura was exposed and opened without any fall in the arterial blood pressure or in the cardiac output. A great deal of trauma was necessary to produce a definite decrease in either the blood pressure or the output of the

TABLE 3.—Results of Trauma to the Cervical Cord, on Cardiac Output and Blood Pressure

Time	Pulse Rate per Minute	Temperature F.	Arterial Oxygen, Volumes per 100 Cc.	Venous Oxygen, Volumes per 100 Cc.	Arteriovenous Difference, Volumes per 100 Cc.	Arterial Blood Pressure		Oxygen Consumption, Cubic Centimeters per Minute	Cardiac Output per Minute, Cc.
						Maximum	Minimum		
1:45 p.m. (90 minutes after exposure of dura).....	98	96.0	19.44	15.00	4.44	124	80	52.71	1187
2:20 (5 minutes after opening dura)	96	19.92	14.28	5.64	110	78	60.62	1075
2:40 (25 minutes after opening dura)	100	94.1	18.84	13.68	5.16	88	78	52.71	1021
3:26 (8 minutes after trauma to cord)	150	18.60	12.24	6.36	64	58	55.35	870
3:52 (34 minutes after trauma to cord)	150	93.8	18.84	11.04	7.80	66	54	47.44	608

heart. When an alteration of this kind was produced, the blood pressure and cardiac output fell together. There was little alteration in the consumption of oxygen. The results of an experiment are recorded in table 4.

PROTOCOL 4: Jan. 1, 1929, weight of dog, 12 Kg.; 9 a. m., 0.098 Gm. morphine; 10:50, control determinations; 12:10, ten minutes after completion of operation for exposure of cord in lower thoracic region; light ether anesthesia, dog awakening at time of observations; practically no loss of blood; dura not opened; 2:45, dura opened for a distance of 3 cm.; dog completely quiet; 2:50, determinations, five minutes after opening dura; 3:15, determinations, thirty-five minutes after opening dura; from 4:05 to 4:08, slight trauma to cord with a blunt instrument; cord not crushed; 4:12, four minutes after trauma, determinations; 4:47, thirty-nine minutes after trauma to cord, determinations; 5:15, sixty-seven minutes after trauma to cord, determinations; 5:30, cord crushed by clamp for distance of about 2.5 cm.; animal struggled little; 5:50, determinations, twenty minutes after crushing cord; 7:15 pulse 188; blood pressure 80 systolic and 64 diastolic.

COMMENT

The data presented here throw some light on the question as to whether or not shock can be produced by trauma to the central nervous system. The operation, the production of the trauma and the collection of the samples of blood for gas analyses resulted in the loss of a moderate amount of blood. The simple removal of the same amount of blood from an animal that did not have the operation and the trauma would not produce changes of the magnitude reported in this paper. The amount of blood lost is comparable to that lost in operations on the central nervous system.

TABLE 4.—*Results of Trauma to the Thoracic Cord, on the Cardiac Output and Blood Pressure*

Time	Pulse Rate per Minute	Temperature F.	Arterial Oxygen, Volumes per 100 Cc.	Venous Oxygen, Volumes per 100 Cc.	Arteriovenous difference, Volumes per 100 Cc.	Arterial Blood Pressure		Oxygen Consumption, Cubic Centimeters per Minute	Cardiac Output per Minute, Cc.
						Maximum	Minimum		
10:50 a.m., control.....	60	96.8	17.88	13.56	4.32	128	66	75.64	1751
12:10 (10 minutes after exposure of cord)	65	96.0	17.40	13.92	3.58	126	68	76.00	2151
2 p.m. (1 hour 50 minutes post-operative)	50	95.8	17.52	13.80	3.72	124	70	84.67	2281
2:45 p.m. (5 minutes after opening dura).....	110	18.12	13.44	4.68	126	74	95.94	2050
3:15 (35 minutes after opening dura)	85	17.28	12.24	5.04	118	64	92.25	1820
4:12 (4 minutes after trauma to cord)	67	17.64	14.28	3.46	122	70	95.94	2772
4:47 (39 minutes after trauma to cord)	160	95.6	17.64	9.60	8.04	98	76	81.18	1009
5:15 (67 minutes after trauma to cord)	158	17.52	10.44	7.08	92	68	70.11	990
5:50 (20 minutes after crushing cord)	175	17.52	8.64	8.88	96	70	73.80	831

Wiggers⁶ studied shock that was produced by manipulation of the intestines, by trauma to the sciatic nerve and testicle and by hemorrhage; he found that the changes in the circulatory mechanism were essentially the same. Blalock,⁷ in a study of the effects of hemorrhage, found that the changes in cardiac output preceded alterations in the mean blood pressure. Usually the maximum pressure fell and the minimum pressure rose before there was a marked reduction in the output of the heart. In the present study, there was a rise in both systolic and diastolic blood pressure, which in some instances occurred immediately after the

6. Wiggers, C. J. (footnote 5); Shock: Abdominal, Initial and Progressive Stages of Circulatory Failure in Abdominal Shock, *Am. J. Physiol.* **45**:485, 1918; Differentiation Between Circulatory Failure due to Shock and Other Causes, *J. A. M. A.* **70**:508 (Feb. 23) 1918.

7. Blalock, Alfred: Mechanism and Treatment of Experimental Shock: I. Shock Following Hemorrhage, *Arch. Surg.* **15**:762 (Nov.) 1927.

trauma and lasted for a few seconds. The cardiac output could not be determined in such a short interval by the method used. After this brief initial period, in a few experiments and in all other instances, it was found that the cardiac output and the maximum and minimum blood pressure declined together. These changes were usually preceded by a definite quickening of the pulse. This is in contrast to the observation in shock produced by hemorrhage. The first change in hemorrhage, with the exception of a lowering of the volume of blood, was a vasoconstriction which caused an increase in the minimum blood pressure. These facts are evidence that vasoconstriction does not occur after injury to the central nervous system. It is also significant that the cardiac output falls tremendously after hemorrhage before the mean blood pressure falls, whereas no instance of a definite fall in cardiac output was found in these experiments with trauma without some fall in the blood pressure. In other words, after trauma to the central nervous system, there is not the critical level in the blood pressure which seems to exist in hemorrhage. This observation probably accounts for the fact that a fall in blood pressure is not as serious during operative procedures on the central nervous system as it is during or after other types of operations or after hemorrhage.

As has been stated previously, the effects of the loss of small amounts of blood cannot be ruled out in these experiments, but the fact that the changes here reported are different from those produced by hemorrhage alone indicates that hemorrhage is not the causative factor. We believe that the results obtained are the results of the trauma to the central nervous system. The rise in the minimum arterial pressure and the fall in the maximum pressure in uncomplicated hemorrhage which results in a lessening of the pulse pressure denotes the onset of a grave condition. The pulse pressure usually maintains a high level during the early stages of trauma to the nervous system, and this is probably a good prognostic sign.

In hemorrhage the blood pressure is not of paramount value as an indication of incipient shock. The blood pressure serves as a more accurate index of the condition of the circulation after trauma to the central nervous system because alterations in the blood pressure parallel other circulatory changes.

The increase in diastolic pressure after uncomplicated hemorrhage in moderate amounts is due to a contraction of the arteries in an effort to keep the arterial blood pressure at the normal level. Undoubtedly there is a different mechanism which operates after trauma to the central nervous system. It is likely that the injury causes a relaxation of the vessels of some large area, such as the splanchnic region, or perhaps of the entire body. The decline in pressure may appear quite early and

probably is not due to the accumulation of toxic products that cause capillary dilatation and increased permeability.

A decline in the blood pressure and cardiac output was found in most instances without any decrease in body temperature. This may be explained in part by the fact that dogs have sweat glands which allow for the dissipation of heat.

Trauma to the nervous system in dogs, accompanied by a decline in the arterial blood pressure and the output of the heart, may or may not be associated with a decrease in the total consumption of oxygen. Henderson, Prince and Haggard⁸ stated that metabolism is lowered in animals in which experimental shock is produced. Aub,⁹ working on cats, produced shock by trauma to the leg in some instances and by hemorrhage alone in others. He stated: "Experimental traumatic shock causes a marked fall in the rate of basal metabolism to 70 per cent of the original level. The degree of fall is dependent on the severity of the shock produced. The effect of hemorrhage is not constant. It may temporarily lower, or have no immediate effect on the metabolic rate." The observations after hemorrhage were confirmed by Blalock.⁷ Cannon¹⁰ emphasized the importance of maintaining the delivery of oxygen to the tissues and stated that most of the harm which results from the low arterial pressure and diminished volume of blood is due to the poor supply of oxygen to the tissues. It is interesting to note in these experiments that the total consumption of oxygen in several instances remained at the normal level, while the blood pressure, the output of the heart and the volume of blood were diminished. Even in instances such as those reported by Aub, in which the basal metabolism fell 30 per cent, the decline can be accounted for partially by decrease in blood flow in the "less essential organs." Gesell¹¹ studied the blood flow through the salivary gland after hemorrhage and injury to the tissues and found striking decreases in the flow. In one experiment, for example, he found that the removal of 10 per cent of the estimated volume of blood caused a decrease of 60 per cent in the flow of blood through the salivary gland. It is likely that a similar condition exists in the extremities.

The volume of the circulatory blood is certainly reduced in shock produced by all methods. Shock may be found with a normal arterial

8. Henderson, Y.; Prince, A. L., and Haggard, H. W.: Observations on Surgical Shock: A Preliminary Note, *J. A. M. A.* **69**:966 (Sept. 22) 1917.

9. Aub, J. C.: Studies in Experimental Traumatic Shock: I. The Basal Metabolism, *Am. J. Physiol.* **54**:388, 1920.

10. Cannon, W. B.: Traumatic Shock, New York, D. Appleton & Company, 1923.

11. Gesell, R.: Studies on the Submaxillary Gland: IV. A Comparison of the Effects of Hemorrhage and Tissue Abuse in Relation to Secondary Shock, *Am. J. Physiol.* **47**:468, 1918.

blood pressure, normal consumption of oxygen, normal pulse rate and a normal temperature. It almost certainly cannot be produced by any method which does not cause a lowering of the cardiac output and of the oxygen content of the mixed venous blood. It is believed that this work emphasizes the futility of trying to designate by the word shock or any other term the varying conditions which result after trauma and hemorrhage. A similar mistake would be the consideration of all fevers as of one type.

SUMMARY

The effects on the pulse rate, temperature, maximum and minimum arterial blood pressures, arterial and venous oxygen content, consumption of oxygen and cardiac output were studied after (1) the operative procedure that was necessary for the exposure of the dura, (2) the opening of the dura, and (3) trauma to the central nervous system in the (*a*) cerebrum, (*b*) cervical cord and (*c*) thoracic cord.

1. In some instances the operation that was necessary for the exposure of the dura and the opening of the dura caused no decrease in the arterial blood pressure or in the cardiac output.

2. Trauma to the central nervous system caused a diminution of the maximum and minimum arterial pressure and the cardiac output.

3. The pulse rate usually increased before the blood pressure and cardiac output altered.

4. The blood pressure and the cardiac output apparently changed simultaneously.

5. The alterations in the consumption of oxygen were variable, but in the majority of instances, trauma caused no appreciable alteration from that of the control period.

6. In the majority of instances, changes in body temperature were negligible.

7. The differences in the effects of hemorrhage and trauma to the central nervous system have been stated.

THROMBO-ANGIITIS OBLITERANS

GENERAL DISTRIBUTION OF THE DISEASE*

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Von Winiwarter,¹ in 1878, described a case in which the arteries of a lower extremity were occluded by a chronic proliferative process arising from the intima and showed an inflammatory reaction of the walls of the vessels. He called this lesion "endarteritis obliterans."

Since then many writers have described this disease, but it was not until the studies of Buerger² in 1908 that the pathologic changes were minutely described and the disease established as a definite clinical and pathologic entity. From the time of the first description by von Winiwarter¹ to the present, there has been a tremendous amount of study and investigation of this lesion.

It is the object in this paper to direct attention to the more general distribution of the disease in contradistinction to what has previously been believed concerning it—that it is a disease involving the blood vessels of the extremities exclusively. It attacks the walls of the blood vessels, both veins and arteries, throughout the entire vascular system, the cranial, thoracic and abdominal vessels as well as the vessels of the extremities. The signs and symptoms are characteristic of the vessels involved, so that the lesion affecting the arteries of the brain may give rise to a hemiplegia, of varying degree of severity, or, should the coronary vessels be involved, the characteristic symptoms of coronary thrombosis or angina pectoris may ensue.

This study is based on thirty-four cases. Twenty-seven were observed by us, including two of hemiplegia in which a definite diagnosis of thrombo-angiitis obliterans had been made and one case of coronary thrombosis in the presence of progressive thrombo-angiitis obliterans. Seven cases were collected from the literature. We have intentionally

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1. Von Winiwarter, Felix: Ueber eine eigentümliche Form von Endarteritis und Endophlebitis mit Gangrän des Fusses, *Arch. f. klin. Chir.* **23**:202, 1878.

2. Buerger, Leo: Thrombo-Angiitis Obliterans: A Study of the Vascular Lesions Leading to Pre-Senile Spontaneous Gangrene, *Am. J. M. Sc.* **136**:567, 1908.

eliminated cases that showed gross arteriosclerotic changes in the vessels to which occlusion of the lumen could be attributed. The patients whose cases we report were under the age of 50 and had shown definite evidence of thrombo-angiitis obliterans for many years. We report these cases because they show a general distribution of the disease. We feel that this is not a large series on which to base conclusions, but we hope that this paper may stimulate further interest and observation.

REPORT OF CASES

CASE 1.—J. S., a Jew, aged 48, born in Russia, was operated on for a duodenal ulcer in 1918 when a gastro-enterostomy was done. His symptoms, however, were not relieved, and six months later he was operated on again. Shortly upon leaving the hospital after the second operation, he began to complain of severe pain in the right calf on walking and more or less constant pain and numbness in the toes of the right foot. In 1921, gangrene developed in the third toe of the right foot. He remained in a hospital in Boston for eleven weeks, when his toe was amputated. The pain in his right leg and foot, however, continued, and shortly afterward gangrene developed in the second toe. At this time, the patient entered the Beth Israel Hospital, where a diagnosis of thrombo-angiitis obliterans was made. An amputation below the knee was done. The stump seemed to heal well and the patient was sent home. Two months later, he came back to the hospital complaining of bleeding hemorrhoids. These bled profusely and produced a severe secondary anemia, which required a transfusion. The hemorrhoids were removed under local anesthesia. At this time, he began to complain of some pain, not severe, in the left calf. Pulsation in the left dorsalis pedis artery was not felt.

The patient got along well with an artificial right limb until June, 1928; then he came back to the hospital because he was unable to raise the stump of his right leg and his speech was slow and thick. On admission to the hospital, he was found to be suffering from a hemiparesis of the right side, involving the right leg and arm and also the right side of the face. The right knee jerk was exaggerated. The abdominal reflexes were abolished. The cremasteric reflex on the right could not be obtained. The blood pressure was 116 systolic and 60 diastolic. The Wassermann reaction of the blood was negative; that of the spinal fluid was negative. His heart was not enlarged. A systolic murmur was heard over the precordia. The aortic second sound was not accentuated.

The paralysis of the right side cleared rapidly. In three weeks, the patient was out of bed and got along pretty well with the support of one crutch. About six weeks after admission, he was discharged from the hospital with a slight residual paralysis.

During his stay in the hospital, the patient had considerable trouble with his left lower extremity, for which he was given sodium citrate. It may be of interest to note a decrease in the pain in the left calf after daily intravenous injections of 20 cc. of a 20 per cent solution of sodium citrate. Another fact of interest is that this patient was not a cigaret smoker; all he ever smoked was three small cigars daily.

Comment.—This patient had a number of vascular accidents. While it is true that a patient suffering from thrombo-angiitis obliterans may have duodenal ulcer, bleeding piles and cerebral thrombosis, the question arises whether all these vascular accidents might not be due to one underlying condition.

In the absence of arteriosclerosis, cardiorenal disease or hypertension, it may be reasonable to suppose that there is a relation between the thrombo-angiitis obliterans of the lower extremities, the presence of which was definitely proved, and the other vascular accidents, and that they are all of the same pathology.

That the disease at the time of writing had not yet become quiescent is shown by the fact that the patient still had intermittent claudication in the left leg and a certain amount of edema and the usual cyanosis of the left foot.

CASE 2.—M. G., a Jew, aged 45, born in Russia, had complained for about a year and a half of pain in both calves on walking, more marked in the right, and extremely severe in the right foot, particularly in the great toe. Examination at the time the pain was first noted showed no pulsation in the dorsalis pedis artery on the right, but it was definitely felt in that on the left. There was a great deal of redness and tenderness of the right toe. The patient was at another hospital for twelve weeks, where a diagnosis of thrombo-angiitis obliterans was made. The pains in his foot were most excruciating, and did not respond to any kind of treatment that was tried, including inoculation with typhoid vaccine. An ulceration of the great toe then began to develop, and an amputation of the leg was considered; however, a ganglionectomy and ramisection were performed, the second, third and fourth right lumbar sympathetic ganglions being removed. The pain stopped immediately, and the ulceration of the toe healed completely. He was discharged from the hospital feeling perfectly well; the pulsation in the dorsalis pedis artery on the right, however, could not be felt.

A few months after he left the hospital, a superficial phlebitis of the right leg developed, which subsided with moderate rest. He soon resumed his work as salesman. While in the West, one day early in August, 1928, he suddenly felt a tingling in his left arm and left leg, which lasted a few minutes. About three quarters of an hour later, he completely lost the power of his left arm and left leg and fell. He was placed on a train and sent on to his home in Boston. He was seen within twenty-four hours after the onset of his trouble. At this time, he had a complete paralysis of the left arm and left leg with a slight involvement of the left side of the face.

Examination.—The physical examination on his entrance to the Beth Israel Hospital on Aug. 10, 1928, showed complete paralysis of the left arm and left leg. Pulsations in the dorsalis pedis artery on the right were not felt, but were felt in that on the left. All the reflexes on the left were exaggerated. A positive Hoffmann's sign was elicited on the left. There was clonus of the left ankle, but no Babinski sign. Abdominal reflexes were active on both sides. There were no sensory disturbances. Examination of the fundus showed considerable tortuosity of the veins, which were rather dark, and the arteries showed a white line around the border. The results of the physical examination were otherwise negative. The heart was not enlarged; the sounds were of good quality without murmurs. The blood pressure was 110 systolic and 80 diastolic. There was no evidence of any renal disease. The Wassermann reaction of the blood was negative. An x-ray picture of the lower extremities showed "no deviation from the normal in the bones and articular surfaces," and "evidence of calcium deposits on the blood vessels around the ankle joints."

The patient felt well and recovered from the paralysis with extraordinary rapidity. A few days after his entrance to the hospital, he had obtained motion in the arm and the leg, and two weeks after entrance he was able to walk.

On August 30, the patient began to complain of pain in the right leg. Examination revealed a superficial phlebitis, characteristic of thrombo-angiitis obliterans, the so-called migrating phlebitis. About four weeks after his admission, the patient was walking, and the grip of his left arm was almost equal to that of the right.

Comment.—This man showed no clinical evidence of arteriosclerosis or cardiorenal disease; he had thrombo-angiitis obliterans with two attacks of superficial phlebitis. A complete hemiplegia developed, which cleared up within so short a time that it could not well have been due to a cerebral hemorrhage. It is interesting to note that the ganglionectomy certainly relieved his symptoms, but apparently did not stop the progress of the disease, as is evidenced by the subsequent history of phlebitis.

The condition at least suggests that the vascular lesion of the brain was similar in character to that of the vascular disease in the legs and that the hemiplegia was probably due to partial occlusion, with vascular spasm of the cerebral arteries, rather than to cerebral hemorrhage.

The fact that the x-ray picture showed evidence of a deposit of calcium in the blood vessels about the ankles is no indication that the occlusion of the blood vessels was the result of arteriosclerosis.³ It simply meant that he was approaching the age when arteriosclerotic changes begin to manifest themselves; it had nothing to do with the disease in question.

CASE 3.—J. M., a Jew, aged 46, married, born in Russia, was referred to the Beth Israel Hospital on Nov. 17, 1928, by Dr. S. A. Levine. Ten years before, the patient had had cramps in the calves when walking. This was diagnosed by Buerger as thrombo-angiitis obliterans. The condition gradually became worse; gangrene of the first two toes of the left foot set in, and one and one-half years before his admission to the Beth Israel Hospital an amputation of both toes was performed. During the few months preceding his admission, the pain in the right leg and right foot became much worse, and a marked change took place in the color of the dorsum of his foot. It was cherry red. Four weeks previous to admission, while in bed, he was suddenly taken with an agonizing pain in the chest of a constricting character, which lasted for thirty-six hours. After this, he had shortness of breath, which he had never experienced previously. On more careful questioning, it was found that for two months previous to the attack mentioned he had had similar minor pains in his chest, which were of short duration. His blood pressure, which varied from 130 to 140 systolic ordinarily, fell to 90 during the attack. Pain was entirely gone when he was last under observation, but he complained of dyspnea, especially at night. When first seen by Dr. Levine, the patient looked sick and dyspneic. His heart was considerably enlarged,

3. Brown, G. E., and Henderson, M. S.: Diagnosis and Treatment of Arterial Vascular Diseases of the Extremities, *J. Bone & Joint Surg.* 9:613 (Oct.) 1927.

and there was a definite sound of pericardial friction and some evidence of congestive failure. The patient when last seen complained of severe pain in the right foot, more particularly in the right great toe.

His other past history and the family history were negative. His wife and three children were living and well.

Examination.—The patient weighed 117 pounds (53.1 Kg.). The vital capacity of his lungs was 1,700 cc. (markedly diminished from normal). The urinalysis was negative. The blood pressure was systolic, 108; diastolic, 70. The Wassermann reaction of the blood was negative. The pupils were equal and reacted normally. The patient looked sick and dyspneic. There was no glandular enlargement. The throat was normal. The lungs showed a moderate number of moist râles at both bases; breath sounds were diminished. The heart was considerably enlarged; the measurements were 13 cm. to the left and 5 cm. to the right. There was a definite fading sound of pericardial friction over the precordia. No endocardial murmurs were heard. There was a question of gallop rhythm. No peripheral edema was observable over the shins or sacrum. No pulsations could be felt in any of the main vessels throughout both lower extremities. The first two toes of the left foot had been amputated. The dorsum of the right foot was cherry red to purple, and the toes felt cold. The radial and ulnar pulses in the upper extremities could be felt. Electrocardiographic tracings showed certain minor changes in the T-wave in lead 1 which are frequently seen in cases of coronary thrombosis. This patient had a ligation of the right popliteal vein. During the operation, the femoral artery as far as it could be felt, showed no evidence of pulsation, nor could pulsation be felt in the popliteal artery.

Comment.—This patient had had thrombo-angiitis obliterans for many years. About ten weeks previous to our study of his case early symptoms of angina pectoris developed. Four weeks previously, he definitely had an attack of coronary thrombosis. The severe pain, the preceding angina pectoris, the fall in blood pressure, the development of dyspnea, the finding of pericardial friction and the change in the electrocardiograms made this diagnosis certain. The right leg, however, when he was last seen, was becoming more painful. The case is interesting especially in that the same condition and the same sequence developed in the coronary arteries that probably were taking place in the arteries of the legs, first the intermittent spasm and finally a closure.

CASE 4 (Riesman⁴).—M. A., a married man, aged 44, a Russian manufacturer, for several years had had a good deal of pain in the epigastrium, for which he had consulted physicians and received various diagnoses, such as duodenal ulcer and that of gallstones. One day Dr. Riesman was asked to see him and found him in an attack characterized by excruciating pain in the epigastrium and profound shock, ending in eventual unconsciousness. The symptoms and physical signs were those of coronary occlusion. The patient died during the attack. On going over his records, Dr. Riesman found that the man had come to him on one occasion several years before, complaining of sciatica. On examination, he found the pulse of the dorsalis pedis artery absent and after close study was able to make a diagnosis of intermittent claudication.

4. Riesman, David: Myocardial Disease and Its Gastric Masquerades, J. A. M. A. 91:1521 (Nov. 17) 1928 (case 3).

Comment.—It was justly assumed that the intermittent attacks of abdominal pain that had led to a diagnosis of gallstones or ulcer had been due to a temporary or permanent occlusion of small branches of the coronary artery; the possibility of a true abdominal angina, an intermittent claudication of branches of the celiac axis, has also to be kept in mind.

CASE 5 (Czerna⁵).—A Polish Jew, aged 36, since the age of 20, had had recurring attacks of pain in the legs, which confined him to bed for from four to six weeks at a time. There were intervals of several years when he was free from pain. He also, at one time, had an "acute attack of heart trouble" for which he remained in bed for four weeks. At one time, paralysis developed in the right side of the face, and lasted for four weeks; at the onset of this attack he also had some difficulty with his speech. At another time, he had an attack of unconsciousness, which was diagnosed as due to a cerebral embolus. The present attack started one year before, when he suddenly began to have severe pain in the left foot and left leg. About three months before his entrance to the hospital, he had an ulcer over the right internal malleolus. A few weeks previous to admittance, he also had an attack of pain in the left arm and hand, which lasted for three weeks.

Examination.—The muscles of the right thigh and the lower part of the right leg were atrophied. Over the right internal malleolus, he had an ulcer about 1 cm. in diameter. There was no edema. The veins were markedly dilated and tortuous. Pulsation in the dorsalis pedis artery and the posterior tibials, on both sides, could not be felt, and there was no pulsation in the right femoral artery. Pulsation in the left radial artery could be felt about 5 cm. proximal to the styloid process; beyond that the artery was felt as a fibrous cord. The heart was slightly enlarged. There were no murmurs. Blood pressure was 130 systolic and 90 diastolic. The urine disclosed nothing abnormal and the Wassermann reaction of the blood was negative. He showed signs of left facial paralysis. His left knee jerk was more lively than the right. There were no sensory disturbances. He remained in the hospital for eight months. After leaving the hospital, he had an attack of severe pain in both feet, and six days later, after the pain had somewhat subsided, he became unconscious, had convulsive seizures and died.

On postmortem examination, it was found that his heart was slightly enlarged and weighed 400 Gm. The wall of the left ventricle was hypertrophied. There were some yellowish-white spots on the left auricle. On the aorta, near the origin of the coronaries, there were a few grayish-white, rough spots. The ascending branch of the left coronary, 3 cm. from the orifice, was occluded by fibrous tissue. Near the orifice of the intercostal vessels were some yellowish spots. The right external iliac and the right femoral were occluded by an organized thrombus. They felt like cords. The left femoral and popliteal arteries were also occluded. The basilar and the beginning of the posterior cerebral arteries were occluded by organized thrombi. The left radial artery about 1.5 cm. distal to the styloid process was occluded by a thrombus. There was an area of softening of the brain about the size of a pea near the corpus callosum and the upper part of the pons.

Comment.—This patient, aged 36, dated his symptoms back to the age of 20. During the progress of his illness, he had had many symp-

5. Czerna, Stephan: Arteritis Obliterans with Similar Changes in the Veins, Arch. f. inn. Med. 12:213, 1926.

toms and physical signs pointing to vascular lesions in the heart and brain as well as in the extremities. The postmortem examination yielded observations consistent with the physical signs presented during life. The lesions characteristic of thrombo-angiitis obliterans were widespread throughout the vascular tree.

CASE 6 (Perla⁶).—A man, aged 44, had begun to complain, at the age of 27, of pain in the left foot; this was followed by gangrene of a toe, which was amputated. Later the other toes of the left foot were amputated, and one year later a midtibial amputation was performed on the left leg. At the same time, he began to have trouble with his right leg, and one year later it was amputated at the upper third of the lower part. Fourteen years after the onset of his trouble, gangrene developed in the ring finger of the right hand, which was amputated. Seven months prior to Perla's observation of the patient, the stump of the left leg began to be painful. It felt cold, was dark blue and soon became gangrenous; it was amputated above the knee. On admission to the hospital at this time, the patient complained of pain in both stumps. A gangrenous patch was observed in the right stump. He suffered from a great deal of pain. Both hands also had a purplish hue and became deeply cyanotic when lowered. When the arms were raised, however, both hands rapidly became pale. The results of the physical examination were otherwise negative. The urine was normal and the Wassermann reaction of the blood was negative. The blood pressure varied between 115 systolic and 90 diastolic and 135 systolic and 92 diastolic. A few months later his right leg was reamputated at the middle of the thigh, and one year later the index finger of his left hand was amputated. One year after this, the patient suddenly had a vomiting attack, became cyanotic and died. On postmortem examination, organized canalized thrombi were found involving the arteries of all the extremities, as well as the external iliac and the left coronary artery. The probable cause of death was thrombo-angiitis obliterans with extension of the process from the iliac arteries into the aorta as far as the renal arteries. The heart weighed 470 Gm. The main left coronary artery, beginning 1.5 cm. from its orifice in the aorta, showed an organized canalized thrombus almost completely occluding the lumen for a distance of 1.5 cm. The process here resembled that in the vessels of the extremities. The right coronary artery showed no abnormalities.

Comment.—The progress of the disease in this patient apparently could not be controlled. Almost all the vessels were involved. At an early age, the patient developed thrombo-angiitis obliterans, which made itself manifest in the lower extremities. Postmortem examination revealed the characteristic lesion of the disease also in the coronary artery.

CASE 7 (Buerger⁷).—A man, aged 35, a Russian, gave a history typical of thrombo-angiitis obliterans of the left lower extremity, for which amputation was

6. Perla, David: An Analysis of Forty-One Cases of Thrombo-Angiitis Obliterans, *Surg. Gynec. Obst.* **41**:21 (July) 1925 (case 3).

7. Buerger, Leo: Concerning Vasomotor and Trophic Disturbances of Upper Extremities, with Particular Reference to Thrombo-Angiitis Obliterans, *Am. J. M. Sc.* **149**:210, 1915 (case 9).

done in 1903, and a reamputation one month later. In 1905, an ulcer developed at the inner side of the right heel. Gangrene advanced rapidly and the right leg was amputated. Five years later, the disease involved the left upper extremity. Gangrene started in his fingers, giving rise to excruciating pain. On the amputation of his forearm, both the radial and the ulnar arteries were completely occluded and showed the typical lesions of thrombo-angiitis obliterans. Four years later, in April, 1914, the patient, in a condition of stupor, was again admitted to the wards of the Mount Sinai Hospital. His speech was incoherent and there were evidences either of some cerebral lesion, or of a vascular lesion in the brain. The condition of the right hand was of particular interest. Nowhere was there any evidence of ulcer or gangrene. The skin of the right hand was dry and atrophic. The fingers had a tapering appearance. The skin had lost its elasticity, the subcutaneous tissues had withered and neither the radial nor the ulnar arteries were palpable. The brachial artery, too, gave but the slightest impression of pulsation.

Comment.—This young man had had several amputations of the lower and upper extremities because of thrombo-angiitis obliterans; signs of a vascular lesion of the brain suddenly developed. In the presence of the known diagnosis, thrombo-angiitis obliterans, and the absence of arteriosclerosis, it may be assumed that the cerebral vascular lesion was due to the progressive activity of this disease.

CASE 8 (Lewis⁸).—A man, aged 47, of German extraction, admitted to the Johns Hopkins Hospital in December, 1926, had for the last seven years had pains in both calves. The pain had increased in severity and frequency, and practically prevented him from walking. Several years after the onset of pain in his legs, the same kind of pain developed in his right forearm, so that he was unable to work. Two years previous to admission, he was operated on for varicose veins, but the pains in his legs were not relieved. The intermittent limping persisted. On examination, the radial pulse could not be palpated on the right side; the left radial pulse was felt faintly, but the arteries were not sclerosed. Both feet were purplish. The dorsalis pedis and posterior tibial arteries could not be felt. The blood pressure could not be obtained on the right arm; on the left arm, it was 136 systolic and 90 diastolic. One night, the patient suddenly became hemiplegic and died.

On postmortem examination, the most interesting condition found was that in connection with the general arterial tree. At the level of the celiac axis, the aorta suddenly became reduced in diameter, so that it measured hardly more than 1 cm. There was an old organized thrombus that totally occluded the abdominal aorta, beginning at the level of the celiac axis and extending all the way to the bifurcation. From about 5 to 8 cm. below the celiac axis there was a small, crescent shaped channel which was the only channel that passed through this portion of the aorta. When a probe was passed through the channel from above downward, the channel was found to end about 5 cm. above the bifurcation, where it communicated directly with a comparatively large branch, which left the aorta and spread out into the surrounding tissue. Below this branch, there was no lumen within the aorta. It was totally blocked by an old organized thrombus, which presented, on section, a peculiar transparent appearance. A complete blockage of the celiac axis had resulted from a comparatively fresh thrombus, which

8. Lewis, Dean: Spontaneous Gangrene of the Extremities, Arch. Surg. 15:613 (Oct.) 1927.

extended from the celiac axis into the lumen of the aorta or, perhaps, in the opposite direction. The portion of the thrombus that was in the lumen of the aorta communicated with the fresh thrombus lying between the exit of the celiac axis and the organized thrombus that filled the abdominal portion of the aorta. The beginnings of the common iliac arteries was occluded by old organized thrombi, which had many channels. The thrombosis affected the internal and external iliac arteries on both sides. The left external iliac artery, just before it became the femoral, was only partially occluded by a thrombus. This was also true of the right external iliac artery. In the femoral artery on the left side, extensive thrombotic changes were seen. None of the branches of the femoral group appeared normal.

In the right femoral region there was extensive thrombosis of the femoral artery and its branches. (All the main branches of the arch of the aorta showed sclerotic changes). A total occlusion of the second portion of the right subclavian artery was found; this extended into the axillary and brachial arteries. The right external carotid was closed by a thrombus; its point of origin from the common carotid was represented by a puckered scar. About 2.5 cm. above the bifurcation of the common carotid, the internal carotid artery was plugged by an organized thrombus, through which passed small, newly developed channels. In the skull, a similar thrombotic process filled the internal carotid at the point of anastomosis with the vessels from the opposite side.

Comment.—The most interesting observation was that, with the lesion so widespread, there was so little evidence of circulatory impairment. Postmortem examination showed to what great extent this disease can be distributed throughout the vascular system.

CASE 9 (Thomas⁹).—A Jewish physician, aged 44, in August, 1918, had a sudden attack of excruciating pain with a sense of constriction in the lower part of the chest. The patient was extremely cyanotic. His pain was so severe that it could be relieved only with $\frac{3}{4}$ grain (0.048 Gm.) of morphine. He remained in bed for ten days with a slight fever. The pulse rate varied from 100 to 120. His physician diagnosed the condition as "angina pectoris." The severity of his pain, however, the cyanosis, the elevation of temperature and the rapid pulse rate made the diagnosis of coronary thrombosis more probable. Three years later, he began to have severe pains in his hips and legs, so that he could not walk even short distances without stopping to rest.

The physical examination revealed conditions essentially normal, except that no pulsations could be felt in the dorsalis pedis, the posterior tibial and the femoral arteries on either side. A diagnosis of thrombo-angiitis obliterans was made.

Comment.—This patient presented a rather unusual clinical picture in that there was an absence of pulsations in the main arterial channels throughout both lower extremities, yet there was no evidence of gangrene. Shortly prior to the attacks of intermittent claudication, he had this severe pain in the chest, which was probably an attack of coronary thrombosis. The story is interesting in that he probably had the same

9. Thomas, H. M., Jr.: Persistent Leucocytosis in the Early Stages of Thrombo-Angiitis Obliterans, *Am. J. M. Sc.* 165:86 (June) 1923.

pathologic process and the same sequence of symptoms in the coronary arteries as in the arteries of the extremities, that is, first spasm and later complete occlusion.

CASE 10 (Telford and Stopford).¹⁰—A man, aged 40, born in England, at the age of 30 had noticed pain in the right calf on walking. Shortly after, a similar pain occurred in the left calf. The pain so increased in severity that for a period of two years he was able to walk only short distances with the aid of crutches. He then noticed that his right leg was slightly swollen and that the toes were purplish. During this time, he had a sore on the front of the ankle, which took eighteen months to heal. Two years before the period in question, however, the left leg began to get worse. The foot was "always stone cold," and a small septic focus appeared on the inner side of the great toe.

Except for a digestive trouble suggestive of duodenal ulcer, his previous condition was good. In his earlier days he had been a most enthusiastic fisherman and had spent much time wading, a habit to which he attributed his troubles.

Examination.—The right leg was much wasted from disuse, the muscle power was good and sensation was everywhere normal. The femoral pulse was normal, but the popliteal pulse was barely to be felt, and there was no pulse below this level. The left foot was dull red; there was edema about the dorsum of the foot and a small onychia of the great toe. There was no pulsation in the femoral artery or at any point below this. One night in January, 1924, this patient was seized with severe abdominal pain, and was found to be suffering from a perforative lesion, presumably of the duodenum, as he had for some time shown symptoms suggestive of duodenal ulcer. Laparotomy was done, and a large perforation of the anterior wall of the first stage of the duodenum was sutured; the operation was completed by posterior gastro-enterostomy. As far as his condition allowed, an exploration was made to ascertain the condition of the intra-abdominal vessels. No pulsation could be felt in the common, internal and external iliac arteries of the left side; these vessels were plainly felt as immobile cords.

He made an excellent recovery from the operation, but in April, 1924, ten and a half years after the onset of the disease, the whole of the left foot rapidly became gangrenous, the condition having spread from the old onychia of the great toe. A supracondylar amputation was done through the left thigh on the following day; the femoral artery at the level of the section was open and normal. The wound healed without incident. The histologic observations were characteristic of thrombo-angiitis obliterans.

Comment.—There was an opportunity to explore the abdominal vessels during life. The exploration revealed an absence of pulsation in the common internal and external iliac arteries of the left side, and these vessels were plainly felt as immobile cords. This man had a duodenal ulcer which perforated. Whether there was any relation between the duodenal ulcer and thrombo-angiitis obliterans is difficult to say, but it is of some significance that in case 1 of our series the patient also had a duodenal ulcer.

Another interesting observation is that, although the common internal and external iliac arteries of the left side were totally occluded, the

10. Telford, E. D., and Stopford, J. S. B.: *Thrombo-Angiitis Obliterans*, Brit. M. J. 2:1035, (Dec. 6) 1924.

femoral artery at the point of amputation was open. This point bears out some observations that we made in our own material—that an organized thrombus may be found in one part of an artery causing occlusion while the vessel slightly above or below this thrombus is perfectly free from obstruction; some distance either above or below this thrombus, another occlusion may be found.

In an interesting and important study, Meleny and Miller¹¹ injected an opaque solution into the vessels of extremities which had been amputated for thrombo-angiitis obliterans and clearly demonstrated the patchy appearance of the vessels. They showed that the opaque mass may fill part of a vessel, leave the artery by a collateral branch and then, by a circuitous route, appear again in the same vessel below.

FURTHER CASES FROM THE LITERATURE

In addition to the cases cited at length, we may also refer to Brown and Henderson's³ two cases of thrombo-angiitis obliterans in young men, both of whom showed evidence of coronary thrombosis.

Lemann¹² had under observation two patients with thrombo-angiitis obliterans both of whom had coronary occlusion.

Buerger, in his book on "Circulatory Disturbances of the Extremities," reported the autopsies in four cases of this disease occurring in young men. He stressed strongly the precocious arteriosclerotic changes in the blood vessels of these patients, particularly in the coronary arteries. One of the patients showed definite occlusion of the mesenteric vessels resulting in gangrene of the intestines. We have purposely not included these cases on account of the fact that there was such gross evidence of occlusion due to arteriosclerosis. However, it seems that in such young persons with a known diagnosis of thrombo-angiitis obliterans of the extremities there might be some relationship between the early atheromatous changes in the visceral vessels and the characteristic lesions of thrombo-angiitis obliterans of the vessels of the extremities.

Oppel,¹³ of Leningrad, called attention to the fact that patients with suprarenal arteriosis¹⁴ sometimes die of intestinal gangrene caused by thrombosis of the mesenteric arteries. He also reported the case of a patient who had thrombosis of the cervical arteries, which caused a hemiplegia. Some patients, he said, die of angina pectoris, and a post-

11. Meleny, F. L., and Miller, C. G.: A Contribution to the Study of Thrombo-Angiitis Obliterans, *Ann. Surg.* **81**:976, 1925.

12. Lemann, I. V.: Personal communication to the authors. The case reports are to appear in the *American Journal of Medical Sciences*.

13. Oppel, V. A.: Spontaneous Gangrene of the Extremities and Suprarenal-ectomy, *Lyon chir.* **14**:1 (Jan.-Feb.) 1927.

14. Oppel uses the term "suprarenal arteriosis" synonymously with spontaneous gangrene and thrombo-angiitis obliterans.

mortem dissection shows that the angina was caused by thrombosis of the coronary arteries. Therefore Oppel concluded that this disease is not local but generalized, and that every artery of the human body may be affected by thrombosis.

Constam¹⁵ also reported four cases of this disease occurring in the upper extremities in young men with no evident involvement of the lower extremities. Koyano¹⁶ in 125 cases found an associated involvement of the upper and the lower extremities in 30 per cent. According to Allen and Brown,¹⁷ of forty patients with definite involvement of the lower extremities twenty-four, or 60 per cent, showed on careful examination either complete or partial closure of the ulnar or radial arteries.

A patient under our observation at the time of writing, who had thrombo-angiitis obliterans, gave a history of intermittent claudication of twenty years' duration and at the time showed nothing more than an ulcer over the terminal phalanx of the left great toe, yet no pulsation in the main arterial channels could be felt throughout the entire left lower extremity. An opportunity was afforded to explore the left external iliac artery for some distance when the left femoral vein was ligated. There was absence of pulsation in the left external iliac artery as far as could be felt. In the right radial artery, the pulsation was much weaker than in the left, and the blood pressure in the left arm was 136 systolic and that in the right 110 systolic. This marked variation in blood pressure and pulsation of both radial arteries, together with the absence of pulsation from the highest point at which the external iliac artery could be felt throughout the entire lower extremity, makes it hard to believe that the disease is limited to the extremities and stops abruptly at the particular point in the external iliac artery that could be felt.

Comment.—From the review of these cases there can remain no doubt that thrombo-angiitis obliterans is a general disease that may attack any part of the vascular system. That it frequently involves the blood vessels of the brain, neck, thorax and abdomen, as well as of the extremities, is proved.

The reason that the characteristic signs and symptoms of thrombo-angiitis obliterans do not appear frequently in the upper extremities and only rarely in other parts of the body may be looked for by analogy

15. Constam, G. R.: Primary Involvement of the Upper Extremities in Thrombo-Angiitis Obliterans, *Am. J. M. Sc.* **174**:530 (Oct.) 1927.

16. Koyano, K.: A Clinical Study of 120 Cases of Thrombo-Angiitis Obliterans Among the Japanese, *Acta scholae med. univ. imp. Kioto* **4**:489, 1921-1922.

17. Allen, E. V., and Brown, G. E.: Thrombo-Angiitis Obliterans: Clinical Study of 200 Cases: Etiology, Pathology, Symptoms, Diagnosis, *Ann. Int. Med.* **1**:535 (Feb.) 1928.

in what takes place in extensive arteriosclerosis in the vascular tree; on postmortem examination in the latter case, one finds marked involvement of the vessels in the upper extremities and in the abdomen, but seldom observes arteriosclerotic gangrene in the upper extremities or lesions in the abdominal viscera. The greater demand made on the circulatory channels of the lower extremities because of static conditions may favor the more rapid development of the lesion. Moreover, the feet are more susceptible to slight injuries from deformities of the nails and from calluses, which are frequently the starting points of gangrene.

We know, moreover, that it is possible to maintain a sufficient circulation to keep up the nutritional balance of a part in the presence of occlusion of the main arterial trunk through collateral or anastomosing branches. If this is true for arteriosclerosis, it is more so for thrombo-angiitis obliterans. For we know from the work of Meleney and Miller,¹¹ of Lewis,⁸ and of Lewis and Reichert¹⁸ that collateral circulation and free anastomosis develop in inverse proportion to the extent and rapidity of the vascular occlusion. For that reason, because the process of occlusion is slower and more gradual in thrombo-angiitis obliterans, there is a tendency in this disease to produce a more liberal collateral circulation.

It might be of interest at this point to compare the symptom complex that occurs as a result of arteriosclerosis of the lower extremities with that from the same condition in the coronary vessels. The earliest symptoms in the lower extremities are usually intermittent claudication on walking a variable distance; the patient complains of severe cramp-like pains in the calves; he must stop and rest before he can continue. Later, there is occlusion of the peripheral vessels and possibly gangrene. A parallel syndrome occurs in sclerosis of the coronary arteries; the earliest symptom is a feeling of constriction through the chest or severe pain over the cardiac area. On exertion, the patient must stop, if walking, and rest before continuing. The later manifestation of coronary sclerosis is a distinct narrowing of the lumen of these vessels or complete occlusion. In thrombo-angiitis obliterans, the symptom complex is, likewise, first partial occlusion and spasm of the vessel causing intermittent claudication, and later complete occlusion. The analysis of the cases cited and the postmortem observations in some of them indicate definitely that a pathologic process similar to that which takes place in the extremities also occurs in the coronary arteries and vessels of the brain.

What we have previously stated in regard to the unusual development of the collateral circulation in the presence of thrombo-angiitis

18. Lewis, D., and Reichert, F. L.: The Collateral Circulation in Thrombo-Angiitis Obliterans, *J. A. M. A.* **87**:302 (July 31) 1926.

obliterans is also true of the blood supply to the myocardium, particularly so in the light of the important work of Gross,¹⁹ who demonstrated that a liberal anastomosis existed between the branches of the coronaries and that the coronary vessels were not terminal end arteries. This work was substantiated later by Spalteholz.²⁰ Oberhelman and LeCount²¹ drew similar conclusions from their studies. The recent work of Wearn²² further demonstrated that there is yet another channel by which the heart muscle may receive a sufficient supply of blood in the face of coronary obstruction; that is, by way of the thebesian vessels.

The question arises: Why do we not see more patients with coronary disease due to thrombo-angiitis obliterans and why has the observation not been made more frequently?

In view of the definitely established fact that the lesions of thrombo-angiitis obliterans do occur in the coronaries, as was shown by the postmortem observations in some of the cases cited, the suggestion is near at hand that the occasional cases of angina pectoris and coronary thrombosis that occur early in life without any evidence of vascular disease elsewhere, may, in some instances, at least, be due to thrombo-angiitis obliterans of the coronaries and not to arteriosclerosis.

The reason that it is not found more frequently on postmortem examination may be that the disease is characterized by a chronic course and that, as years go on, arteriosclerotic changes also take place in the vessels affected by thrombo-angiitis obliterans. The latter may be entirely overlooked in the presence of arteriosclerosis.

PATHOLOGY

From our studies of the gross pathologic changes of this disease, we have noted not infrequently that an organized thrombus may be found in one part of an artery causing occlusion and the vessel slightly above or below this thrombus be found perfectly free from any obstruction; some distance either above or below this thrombus another occlusion may be found. This would tend to show that the disease does not start from one special focus in a vessel, but rather arises at various levels, at different periods. This observation is based on the microscopic observations which, for example, as in one of our cases, show a well organized thrombus in the posterior tibial artery and a subacute lesion in the lower end of this vessel. These observations tend to indicate that this disease is disseminated by the blood stream.

19. Gross, L.: *The Blood Supply to the Heart, Its Anatomical and Clinical Aspects*, ed. 1, New York, Paul B. Hoeber, 1921.

20. Spalteholz, W.: *Die Arterien der Herzwand*, Leipzig, S. Hirzel, 1924.

21. Oberhelman, H. A., and LeCount, E. R.: *Variations in Anastomosis of Coronary Arteries and Their Sequences*, J. A. M. A. **82**:1321 (April 25) 1924.

22. Wearn, J. T.: *The Role of the Thebesian Vessels in the Circulation of the Heart*, J. Exper. Med. **47**:293 (Feb. 1) 1928.

It is probable that the disease attacks the larger vessels first, then, in the late stages, obliterates the arterioles and capillaries. This is shown by the fact that gangrene does not occur, as a general rule, until late in the disease. We know from the studies of Meleney and Miller²¹ and the observations of Lewis⁸ that there is a vigorous attempt at the formation of a collateral circulation to compensate for the occlusion of the larger vessels. It would be necessary, therefore, for the smaller arterioles and capillaries to hypertrophy and dilate to take care of this circulation; it is not unusual for this disease to exist for many years with no evidence of impairment of the circulation, although pulsation in the dorsalis pedis and posterior tibial arteries is absent. This points out that the circulation is taken on by the small arterioles, and that for some unknown reason the larger vessels suffer most, although some of the smaller vessels no doubt are also attacked late in the disease.

The collateral circulation in this disease evidently plays the most important rôle, and the ability of the arteries to make and produce new and larger collaterals often is the deciding factor as to whether or not the patient will lose a member. The mechanism of the formation of collateral circulation is not altogether obvious or easily explained. It is a remarkable phenomenon that the main arterial channels become totally occluded without the part becoming gangrenous. Clinically, it is well recognized that with occlusion of the main vessels the collateral circulation has taken the place of the main arteries. Bolognesi²³ performed experiments to determine the effect of ligating the external iliac artery in dogs. He found that the gluteal branches of the iliac artery, and especially those of the inferior or ischiatic gluteal artery, took part in the formation of the collateral circulation, becoming larger and richer in branches. These branches anastomosed fully with the femoral branches. Bernheim and Sachs,²⁴ in studies on the collateral circulation of the lower extremities of patients examined post mortem, found that the circulation to the extremities, even though the femoral artery was occluded above the origin of the profunda femoris, could be taken care of by way of the gluteal arteries in the presence of profound arterial disease. They observed in cases in which this condition existed that the gluteal vessels grew much larger and that they offered a direct line of blood flow to the tissues of the lower part of the leg and foot through the branches that run along with the sciatic nerve. In normal limbs these branches were almost invisible. That this can be accomplished is evidenced in a case reported by Dumas and Ravault,²⁵ in which the

25. Dumas, A., and Ravault, P.: *Physiologic and Histologic Investigations on the Circulatory Conditions in the Left Leg, the Femoral Artery of Which Had Been Ligated in 1870*, *Lyon chir.* **24**:387 (July-Aug.) 1927.

23. Bolognesi, quoted by Buerger (footnote 27).

24. Bernheim, B. M., and Sachs, L.: *Notes on the Collateral Circulation in Blood Vessel Diseases of the Lower Extremities*, *Ann. Surg.* **86**:417 (Sept.) 1927.

femoral artery had been ligated in the upper part of Scarpa's triangle fifty-six years before. The patient was a man who had been wounded in the left leg by a bursting shell in the Franco-Prussian war of 1870. He was examined prior to his death, which occurred on Nov. 21, 1926. There was no evidence of vascular disturbance at that time. At autopsy, it was found that an adequate collateral circulation had been established, so that the femoral artery shortly below the ligature was of normal caliber and the popliteal, anterior and posterior tibial arteries were the same on one side as on the other.

The veins in thrombo-angiitis obliterans present a condition similar to that of the arteries. Some authors² stated that about 30 per cent of their patients showed a superficial phlebitis; occasionally one sees a deep phlebitis that is characterized by more or less edema, which some investigators²⁶ use as a sort of indicator as to whether an amputation should be done above or below the knee. A superficial phlebitis developed in one of our patients while he was in the hospital (case 2). This was probably the condition that Buerger²⁷ referred to as migrating phlebitis.

Pathologic Histology.—The pathologic changes are characteristic and certainly indicate that the initial process is inflammatory. One first notices in a vein a fresh clot made up of polymorphonuclear leukocytes, lymphocytes, mononuclear leukocytes, wandering cells and red corpuscles. As the lesion progresses, foreign body giant cells are seen. This phase is present in veins in which superficial phlebitis has occurred. Attention was directed to these foreign body giant cells first by Buerger.²⁸ The inflammatory cells soon invade the intima, media and adventitia, so that in the process of healing the vein, artery and nerve are closely bound together by the newly formed inflammatory tissue. This tissue soon becomes well organized, and it is with difficulty that the vein, artery and nerve are separated. This process appears to be a phase of a defense reaction that occurs in inflammation and is really a reparative process.

Since it has been proved¹⁷ that there are no changes in the blood to cause the formation of a clot or thrombus, it is fair to assume that the clot is due to trauma to the inner wall of the vessel. As this characteristic clot, made up of fibrin, polymorphonuclear leukocytes, wandering cells, mononuclear leukocytes and giant cells, begins to organize, strands of fibrous tissue arise from the periphery made up of young connective tissue cells, mostly fibroblasts. This process goes on until there is

26. Allen, E. V., and Meyerding, H. W.: *Surgical Procedure in Obliterative Vascular Disease (Thrombo-Angiitis Obliterans): A Report of 45 Cases*, Surg. Gynec. Obst. **44**:260, 1928.

27. Buerger, Leo: *Circulatory Disturbances of the Extremities*, Philadelphia, W. B. Saunders Company, 1924, p. 214.

28. Buerger (footnote 27, p. 320).

complete organization of the clot. In the process of the connective tissue change there are formed new small blood vessels lined by a single layer of endothelium and somewhat similar to the capillaries in healed or healing scar tissue. The pathologic picture is entirely that of an inflammatory process with the characteristic picture of healing. This process keeps repeating itself in various vessels at various levels and at different times, so that the condition is characterized by chronicity, and it is this chronic inflammatory process that slowly occludes the vessels. It has aptly been described, therefore, as a race between the formation of a collateral circulation and the occlusion in the main arterial channels. That this process is characterized by chronicity is proved by the fact that some patients with this disease have dated their symptoms back twenty years. We had one patient in our series who was positive that he had had symptoms of intermittent claudication for fully twenty years before the onset of the trophic disturbance.

SUMMARY

This study covered thirty-four cases of thrombo-angiitis obliterans; twenty-seven cases came under our own observation and seven were collected from the literature. All the cases occurred in persons under 50 years of age, who had had the disease for many years previous to the manifestations of definite nutritional disturbance. None of the patients, therefore, were of the "arteriosclerotic age" when the disease started. In the postmortem examinations which we collected, in which evidence of arteriosclerosis was found, the arteriosclerotic process was obviously not responsible for the condition, but had been superimposed on the long standing thrombo-angiitis obliterans.

An analysis of our material shows that the disease is of a slow, insidious onset, and of many years' duration. The vessels involved are slowly occluded and, owing to this slow occlusion, there is an opportunity for collateral circulation to be established. This explains the fact that the nutrition of the part supplied by the occluded vessel is maintained, and a patient may go on for many years without nutritional disturbance of the parts involved. We have also seen that the process in the arterial tree does not spread by extension from a single focus, but may occur at different levels in an artery and in various vessels at different periods.

Above all, the analysis of our cases, and of those collected from the literature in which necropsies were performed, demonstrates that this disease is not confined to vessels of the extremities, as is generally accepted, but is a generalized disease that may affect any part of the arterial tree, including the coronary arteries, the abdominal arteries and the arteries of the brain.

THIRTY-NINTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY*

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CONGENITAL DEFORMITIES

Congenital Dislocation of the Hip.—MacAusland¹ reviewed the history of the operative treatment of congenital dislocation of the hip. According to him, the patients who should receive operative treatment are: (1) children from 4 to 8 years of age, in whom one or two closed manipulations have failed; (2) children over 8 years of age, and (3) adults with marked deformity or arthritic symptoms. The choice of operation depends on the existing deformity and to some extent on the age of the patient. Simple replacement of the head into the acetabulum, or some form of reconstruction operation with or without the formation of a shelf, or arthrodesis are the procedures one has at one's disposal. The author describes in detail his operative technic and the postoperative care of the patient.

NUTRITIONAL DISTURBANCES

Activated Ergosterol.—An editorial in *The Journal of the American Medical Association*² says that recent studies of Rosenheim and Web-

* Submitted for publication, Sept. 12, 1929.

* This Report of Progress is based on a review of 238 articles selected from 390 titles dealing with orthopedic surgery appearing in medical literature between Feb. 15, 1929, and June 1, 1929. Only those papers which seem to represent progress have been selected for note and comment.

1. MacAusland, W. R.: *Surg. Gynec. Obst.* 47:697 (Nov.) 1928.

2. Editorial: The Precursor of Vitamin D: Ergosterol, *J. A. M. A.* 91: 1110 (Oct. 13) 1928.

ster in London make the position of ergosterol as a parent substance of vitamin D appear unique. They have presented evidence which strengthens the assumption that only a molecular structure such as that possessed by ergosterol enables an esterol to be photochemically converted into vitamin D, and confirms the evidence already available for the view that ergosterol is the specific parent substance of vitamin D. Fortunately, the substance is obtainable with comparative ease from natural sources, so that there need be no limitations to its availability for therapeutic use if this is finally established on a sound basis.

Karelitz³ discussed the value of ergosterol, a substance formerly isolated from mushrooms, ergot and yeast, when activated by a magnesium spark of a mercury vapor quartz lamp. He cited evidence to prove that it is 20,000 times as effective as cod liver oil in combating rickets.

Hess, Bills and Honeywell,⁴ studying the variability of the antirachitic potency of cod liver oil, found that contrary to current opinion, this varies inversely with the amount of oil in the livers. From extremely "poor" livers, oil was extracted which was 200 times more potent than high grade cod liver oil and far more potent than any oil heretofore assayed. The oil from livers of individual cod may vary 1,000 times in their antirachitic value.

Renal Rickets.—Kellet⁵ reported a case of renal rickets in which the inorganic phosphorus in the blood was below normal (3.82 mg. per hundred cubic centimeters). The blood urea was 158 mg. and the calcium 10.4 mg. It has been suggested that the bone changes in renal rickets are due to an increased retention of phosphorus because of the failure of the kidney to excrete phosphorus. This case appears to refute this view. Kellet reported benefit in this case from ultraviolet therapy, whereas in most cases of renal rickets the patients are made worse by actinotherapy.

DISTURBANCES OF GROWTH

Displacement of the Upper Femoral Epiphysis.—In a review of twenty-seven cases of displaced upper femoral epiphysis, Badgley⁶ expressed the belief that at adolescence there is a change in the anatomic relationship of the head to the neck of the femur, and that there may be a thinning of the periosteum at the time of puberty, as pointed out by Key. These factors plus obesity and rapid growth, which are char-

3. Karelitz, S.: Activated Ergosterol in Treatment of Rickets, *Am. J. Dis. Child.* **36**:1108 (Dec.) 1928.

4. Hess, A. F.; Bills, C. E., and Honeywell, Edna M.: Antirachitic Potency in Relation to Volume of Oil in Liver of Cod, *J. A. M. A.* **92**:226 (Jan. 19) 1929.

5. Kellet, C. E.: *Proc. Roy. Soc. Med.* **22**:142 (Dec.) 1928.

6. Badgley, C. E.: Displacement of Upper Femoral Epiphysis, *J. A. M. A.* **92**:355 (Feb. 2) 1929.

acteristic of these patients, are important. The endocrine dysfunction is, he thinks, of little significance. The necessity of early treatment is emphasized. In the preslip stage he advised a plaster spica with the hip in abduction and internal rotation for six weeks and then the use of a walking caliper. The cases in which displacement has occurred recently require the Whitman manipulation, a plaster spica for five weeks, at the end of which time physiotherapy is started. At the end of eight weeks, a splint is given and the patient allowed to walk. In cases in which the epiphysis has been displaced as long as four months, Badgley would employ the curved osteotomy of Wilson. In young adults in whom healing has occurred the Whitman reconstruction operation is required, while in older patients fusion seems the best method of treatment.

[ED. NOTE.—Obesity is not always a characteristic of this condition, and we are not prepared to say that endocrine dysfunction is of little significance. As yet we know too little of this condition to make such statements.]

Achondroplasia.—Warner⁷ described and gave illustrations of twins, aged 10½ years, one of whom was an achondroplastic dwarf and the other a normal child. He argued from this that achondroplasia is an inherited variation and is not due to any maternal infection or influence.

VASCULAR DISEASES

Thrombo-Angiitis Obliterans.—Allen and Smithwick⁸ reported their results in twenty-five patients with peripheral vascular disease, treated by foreign protein shock. Two of the cases were undoubtedly of vasomotor origin; thirteen were of presenile gangrene, clinically thromboangiitis obliterans; six were of arteriosclerotic gangrene, including those with associated diabetes; and four were unclassified. Nineteen patients were admitted with ulceration, only six had pulsating vessels, and nineteen were completely disabled. The number of treatments varied from one to fifteen over periods varying from three weeks to fifteen months, without deleterious effect on the patient. Of the nineteen patients entering with complete disability, five had major amputations and are included in the group of seven patients considered as unrelieved. Twelve of the nineteen patients with complete disability have been able to return to their former work. Nonspecific foreign protein (typhoid vaccine given intravenously) gives a definite reaction much like that observed following periarterial sympathectomy with a definite relief from pain and a beneficial change in the appearance of the lesions. The reaction can be repeated at intervals of seven days

7. Warner, Allan: Brit. M. J. 2:983 (Dec. 1) 1928.

8. Allen, Arthur W., and Smithwick, R. H.: Use of Foreign Protein in Treatment of Peripheral Vascular Diseases, J. A. M. A. 91:1161 (Oct. 20) 1928.

or more with subsequent healing of the ulcerations. The treatment should be combined with proper hygiene and minor surgical operations when necessary, as it enhances the safety of such procedures.

The end-results in ninety periarterial sympathectomies were reported by Muller.⁹ In arteriosclerotic patients twelve operations were performed, two of these being relieved from pain. In no cases of arteriosclerosis was gangrene checked by sympathectomy. Seventeen operations were performed for thrombo-angiitis obliterans. Two of these were followed by definite improvement. Pain was relieved, but no increase in the circulation was found. The operation was performed in three cases of Raynaud's disease with relief from symptoms in two of the cases. The author expressed the belief that the operation is of particular value in chronic ulcers of the extremities which have not yielded to the usual therapeutic measures.

Archibald¹⁰ found that pain from arterial disease of organic origin was not relieved by periarterial sympathectomy in more than half his cases. Ramisection was necessary in some to relieve pain.

Philips¹¹ reported a number of cases of neurocirculatory disease in which roentgen treatment was given. He stated that irradiation given over the spinal segments controlling the affected parts overcomes an overirritated status of the sympathetic ganglions. Relief from pain may occur immediately or several weeks later, followed by improvement in the circulation.

[ED. NOTE.—These reports are significant in that they show the widespread interest in conservative measures as against amputations in vascular diseases of the extremities. The last report is of an untried field, as far as we are aware, and should be repeated by other roentgen therapists.]

NEUROLOGIC CONDITIONS

Traumatic Ulnar Neuritis.—Platt¹² divided ulnar neuritis into the following clinical groups:

1. Primary neuritis resulting from contusions of the nerve or from supracondylar fracture or dislocations of the elbow.
2. Secondary neuritis complicating fractures of the lower end of the humerus or dislocations of the elbow.
3. Delayed neuritis, a sequel to external condyle fractures or caused by recurrent dislocation of the nerve.

In the milder forms of neuritis, resting the nerve in a relaxed position usually suffices; but in the severe form, the operative treatment

9. Muller, G. P.: *Ann. Surg.* 88:474 (Sept.) 1928.

10. Archibald, E.: *Ann. Surg.* 88:499 (Sept.) 1928.

11. Philips, H. B.: *M. J. & Rec.* 128:559 (Dec. 5) 1928.

12. Platt, Harry: *Surg. Gynec. Obst.* 47:822 (Dec.) 1928.

is usually indicated. The technic of anterior transposition of the nerve is described in detail. Special emphasis is placed on preservation of the small branches of the nerve and its blood supply, and on careful fixation and protection of the nerve in its transplanted position.

Surgery of the Sympathetic System.—Leriche¹³ concluded from his observations that the sympathetic nervous system acts like a vast sensory cistern with reflex associations everywhere. Every section of a sympathetic chain is followed by active vasodilatation that is more or less lasting. Paresis of vessels never occurs. Section, also, is always followed by cicatricial neuroma. The author reports the results in 400 cases of ganglionectomy, ramisection and arterial sympathectomy. Gratifying results are reported in the neuralgias following severe injuries or amputations of limbs and in chronic ulcers.

Von Lackum¹⁴ found no reason to withdraw his statement of 1926 that "there is no longer any doubt as to the efficacy of sympathetic ramisection in certain cases of spastic paralysis." Fifty-four lumbar and ten cervical ramisections have been performed. Good results can be obtained only in patients with the best mentality. Von Lackum felt that this procedure offers an effective means of relief in many cases of spastic paralysis in children.

TUBERCULOSIS

Roentgen Diagnosis.—Ghormley and Bradley,¹⁵ who believe that the study of a single roentgenogram of a tuberculous spine is of interest from a diagnostic standpoint, but from a prognostic standpoint is of much less value than a series of roentgenograms on the same patient, gave the result of their study of seventy such pictures taken at the New England Peabody Home for Crippled Children. These pictures were taken at four month intervals over a period of from two to five years or more. The patients have for the most part been treated by conservative methods—recumbency during the early stages of the disease, combined with heliotherapy, fresh air and the usual modern requisites in good general care of tuberculous patients. These estimates would therefore probably vary somewhat in a series of cases in which operation had been performed.

From this study the writers concluded that:

1. Calcification in a lesion does not necessarily mean satisfactory healing.

13. Leriche, R.: *Ann. Surg.* 88:449 (Sept.) 1928.

14. Von Lackum, H. LeRoy: *Sympathetic Ramisection in Spastic Paralysis*, *J. A. M. A.* 92:139 (Jan. 12) 1929.

15. Ghormley, Ralph K., and Bradley, John I.: *J. Bone & Joint Surg.* 10:796 (Oct.) 1928.

2. Clearing or reestablishment of bony detail is a much better indication of healing.

3. Bony fusion or bony block is a favorable sign.

4. Decrease in the size of the abscess is a favorable sign, while increase in the size of the abscess is decidedly an unfavorable sign.

5. Paravertebral abscesses accompanying dorsal Pott's disease are dangerous in that they cause a much wider destruction than the original lesion. A mechanical pulsating force must play a part in their production.

6. It is suggested that early eradication of such abscesses might be attempted, but the danger of establishing a permanent sinus is serious.

Treatment.—Clavelin and Sicard¹⁶ advocated the use of intravenous administration of calcium chloride followed immediately by ultraviolet irradiation. This was suggested to them by the work of Weill and Guillaumin on calcium fixation. They have worked out a definite dosage and plan of treatment, and feel that they have had favorable results in twenty-eight cases.

POLIOMYELITIS

Use of Convalescent Serum.—According to Aycock, Luther and Kramer,¹⁷ the rationale of giving convalescent serum in poliomyelitis is based on three facts:

1. One attack of poliomyelitis apparently confers immunity from the disease.

2. The blood serum of human beings and of monkeys who have had the disease neutralizes the virus.

3. Convalescent serum when tested experimentally exerts a protective action against the virus.

The blood, after fever and muscle tenderness have subsided, is collected into a special bottle (from 400 to 500 cc. from adults and from 200 to 300 cc. from children). It is then incubated for one hour at 37 C., and the serum is drawn off into an aspirating bottle. The serum is given both intraspinally and intravenously. Twenty cubic centimeters of the spinal fluid is withdrawn, and the same amount of serum is introduced into the spinal canal; following this, 60 cc. of the serum is given intravenously. The intraspinal dose is repeated the following day, and if the fever persists, the intravenous dose may again be given. Reactions are frequent but usually not severe.

Tendon Transplantations.—Naughton Dunn,¹⁸ in his presidential address to the orthopedic section of the Royal Society of Medicine,

16. Clavelin and Sicard, André: Presse méd. 36:227 (Feb. 22) 1928.

17. Aycock, W. L.; Luther, Elliott H., and Kramer, S. D.: Technic of Convalescent Serum Therapy in Poliomyelitis, J. A. M. A. 92:385 (Feb. 2) 1929.

18. Dunn, Naughton: Proc. Roy. Soc. Med. 22:243 (Dec.) 1928.

London, on the surgery of the muscles and tendons in relation to infantile paralysis, emphasized the fact that division of tendons and muscles is seldom necessary for the correction of deformity. In Dunn's opinion, no tendon should be divided or lengthened unless the surgeon is satisfied, as a result of his experience, that (1) correction of the deformity will improve function; (2) elongation or division of tendons is necessary to correct that deformity, and (3) the power of the shortened muscle or tendon cannot be utilized by tendon transplantation at the time of the operation. Dunn quoted flexion deformity of the hip to illustrate this axiom. The operative correction for flexion deformity of the hip joint that is commonly advised weakens the tensor fascia femoris and the gluteus medius; and yet no splintage can mask the limp resulting from paralysis of the gluteus medius, and Legg's operation of transplanting the tensor fascia femoris is the usual operation recommended to replace its function. Dunn therefore strongly urged the gradual correction of flexion contracture of the hip, thereby preserving muscles that might be badly needed for transplantation. Dunn stated that the successful transference of muscle power to a new insertion, given a good surgical technic, is mainly dependent on the recognition of the group action of muscles. In the foot, for example, there are for practical purposes only two groups of muscles: (1) the anterior tibial, in action in dorsiflexion of the foot; (2) the peroneal and posterior tibial muscles, associated in action with the tendo achillis in plantar flexion. Any of the anterior tibial muscles can successfully replace one another, but no tendon from the peroneal or posterior tibial group will effectively replace the loss of active dorsiflexion. In the upper limb where the action of individual muscles is more specialized, reeducation of an individual tendon to act apart from its group is more practicable. In the technic of transplantation, Dunn expressed the belief that the important factor is the degree of tension under which the tendon is sutured. The method of attachment—whether to bone periosteum or tendon—and the preservation of the tendon sheath, he considers of minor importance. For weakness of the tibialis anticus, Dunn performs the operation he calls "tendon fusion." All the anterior tibial tendons above the ankle are sutured together, the tension on individual tendons varying according to the previous tendency to inversion or eversion of the foot. While recognizing tendon transplantation as helpful, Dunn expressed the belief that it does not by itself produce spectacular success and that joint fusions are frequently needed in addition.

[ED. NOTE.—Naughton Dunn's observations on lengthening muscles in infantile paralysis are well taken.]

PYOGENIC INFECTIONS

Osteomyelitis.—Phemister,¹⁹ writing on the unusual forms of osteomyelitis, listed sclerosing osteomyelitis, localized diaphyseal osteomyelitis, nonsuppurative or fibrous osteomyelitis, chronic hemorrhagic osteomyelitis and osteitis fibrosa cystica. In sclerosing osteomyelitis, there is a wide diffusion of the infection without necrosis. Pain of varying intensity is the only symptom, and the patient is usually relieved by opening the sclerosed bone. Localized osteomyelitis in the shaft may be acute or chronic; pus is found only very early, and later the necrotic tissue is replaced by fibrous tissue. Areas of nonsuppurative osteomyelitis develop rather silently and are often mistaken for neoplasms. In chronic hemorrhagic osteomyelitis, the diseased tissue is stained brown from the blood pigments. It runs a chronic mild course, and the walls of the diseased area show the signs of an inflammatory process. Osteitis fibrosa cystica may be single or multiple and usually appears during the growing period. The walls of such cysts are definitely inflammatory. It is often difficult to differentiate such tissue from benign giant cell tumor.

ARTHRITIS

The Synovial Fluid in Arthritis.—Forkner, Shands and Poston²⁰ studied the bacteriology and cytology of the synovial fluid in sixty-three cases of chronic arthritis. Of these fifty-two were infectious, nine hypertrophic and two both infectious and hypertrophic arthritis. Organisms were recovered in fourteen cases, eleven of these being *Streptococcus viridans*, two the gonococcus and one *Staphylococcus aureus*. Bacteriologic examination of the regional lymph nodes gave positive cultures in 48 per cent. The cells in the synovial fluids of thirty-three patients were studied by the supravital technic. The polymorphonuclear neutrophils were increased in all cases, when organisms were recovered from the fluid. In synovial fluids in which no organisms were obtained, the monocytes and lymphocytes gave higher counts.

Deformity of Knee in Arthritis.—Swaim²¹ pointed out that the commonest deformity of the knee in arthritis is flexion and subluxation with outward rotation. This deformity presents a grave problem in the plan of reconstruction of the chronic arthritic patient as, no matter what procedures one may use—conservative stretching, manipulation or operation—only rarely is the knee a complete functional success. Flexion deformities can be prevented early in the disease and so simply that it can be done by any one. Swaim believed that if more care

19. Phemister, D. B.: Northwest Med. 27:460 (Oct.) 1928.

20. Forkner, C. E.; Shands, A. R., and Poston, M. A.: Synovial Fluid in Chronic Arthritis, Arch. Int. Med. 42:675 (Nov.) 1928.

21. Swaim, Loring T.: J. Bone & Joint Surg. 10:742 (Oct.) 1928.

were exercised in the beginning of the active arthritis to foresee and prevent this one deformity, most patients with chronic arthritis would be on their feet much earlier than at the present time is possible. These deformities can be prevented by the use of properly applied plaster casts which should be bivalved and used at night and supplemented during the day with active exercise or a cuff with a heavy elastic band applied to the upper end of the tibia attached to a Balkan frame which takes away the mechanical force that causes the deformity.

MISCELLANEOUS

Fundamental Conceptions in the Understanding of Pathologic Change in the Bone.—Leriche and Policard²² discussed the four fundamental principles which in their opinion must henceforth govern all investigations of pathologic change in the bone.

1. Bone tissue must be considered as a storehouse of mineral matters (subject to the fluctuations of the circulation). A large part of pathologic change in the bone must be regarded as resulting from anomalies or derangements of the mineral reserve function. In order to understand this it is essential to know by what physiologic process the mineral reserves that constitute bone are built up or torn down. The authors believe that variation in the blood supply plays a large part in causing withdrawal of calcium. By experiment, they have been able to demonstrate that increase of the circulatory activity in the region of a bone is followed by rarefaction of that bone, e. g., by ramisection or periarterial sympathectomy there is produced an intense vasodilatation with decalcification of the bone. Since active vasodilatation produces an excessive withdrawal of mineral matter from the bone, they conclude: (1) that active vasodilatation is the physiologic mechanism employed by the organism where it needs calcium; (2) that the organism when it needs mineral salts extracts them from the reserve supply by waves of vasodilating nerve impulses and (3) that all diseases either general or local which provoke active vasodilatation must cause decalcification of the bones in that region. They point to the phenomena of decalcification that are observed in pregnancy, in phosphate poisoning and after traumatism as confirming these hypotheses. They also consider such lesions as Kienbock's disease, Kohler's disease and tarsal scaphoiditis as of vasomotor origin, characterized by a moderate rarefaction, spontaneously curable but with dysharmonic-osteogenic processes of repair.

2. The laws of osteogenic reconstruction in the adult govern anatomically the evolution of diseases of bone.

22. Leriche, R., and Policard, A.: Presse méd. 36:1282 (Oct. 10) 1928.

According to the authors, the fundamental principle is that at the beginning of every process of ossification there is produced an active hyperemia, acting simultaneously on the bone and on the adjacent soft tissues. This provokes a rarefaction of the former and an edema of the latter. The rarefaction sets free mineral salts, but as the ability of the blood to transport calcium is fixed at a constant, these salts become deposited in the adjacent soft tissues which have been prepared by the edema for participation in the reparative process. The same process applies to pathologic ossification whether resulting from infection or not.

3. Bone not only is a storehouse for minerals, but is also a hemato-poietic organ.

According to the authors, the bone marrow has nothing to do with the phenomena of ossification or with the life process of bone. The reactions of bone and of the bone marrow are entirely independent.

4. The mechanism of growth in length of bone is purely of cartilaginous character.

The authors stated the belief that growth in length is bound up with a balance between two phenomena of inverse character which follow each other without ever stopping: the growth of cartilage and its destruction by the bone. If the cartilage cells cease to multiply, growth stops. If the cartilage fails to obtain nourishment, ossification does not take place and again growth stops. The cartilage is nourished by imbibition; its diseases are only trophic disturbances. Because of the absence of blood vessels, the cartilage is only affected by means of its exchanges even in infection and inflammation. Finally, the life and the death of the cartilage are regulated by endocrine influences. All diseases of growth of bone and the dystrophies of the epiphyseal cartilage ought to be studied in the light of these considerations.

[ED. NOTE.—Leriche and Pollicard have for a long time been profound students and active experimental investigators of the physiology of bone. The views expressed in the foregoing paragraphs represent a crystallization of ideas which have been previously expressed at greater length and more detail in book form. They support the physioclinical theory of ossification as contrasted with the osteoblastic cellular theory. While many of their ideas are purely speculative and their conclusions open to question, every one who is familiar with their work will admit its scholarly quality and its background of studious investigation and careful observation. All physicians who are interested in bone surgery should read their interesting and thought provoking book, *The Physiology of Bone*.²³]

23. Leriche, R., and Pollicard, A.: *The Normal and Pathological Physiology of Bone: Its Problems*. Translated by Sherwood Moore and J. Albert Key, St. Louis, C. V. Mosby & Company, 1928, pp. 236.

Myofascitis.—Albee²⁴ defined myofascitis as a local manifestation of a general toxic condition, evidenced by a low-grade inflammation or toxic involvement of the muscles and fasciae, the symptoms predominating at the fascial insertions of muscle to bone. He has found it a prevalent condition and considers it a frequent cause of backache often misdiagnosed as sacro-iliac strain, lumbago, sciatica and muscular rheumatism. In his experience the evidence has indicated the colon as the source of the toxic absorption in 90 per cent of the patients, and the teeth, tonsils, sinuses, and gallbladder in the remaining 10 per cent. He has obtained striking relief of symptoms by removal of the toxic absorption from the colon, often in patients who had been entirely unrelieved by mechanical and supportive treatment of the spine.

[ED. NOTE.—Myofascitis as described by Albee may exist, but its presence is difficult to prove. Unfortunately, there is scarcely ever any chance of investigating the pathologic changes at necropsy. In cases such as these, it is almost impossible to rule out a mild toxic or infectious arthritis of the spine in a stage too early to show proliferative bone changes by roentgen examination. Measures susceptible of relieving the one ought also to benefit the other. Whether we call it myofascitis or arthritis, we can at least agree on the necessity of removing foci of infection and eliminating intestinal absorption in many cases of painful back.]

Volkman's Ischemia.—Robert Jones²⁵ clinical experience agrees with the experimental observations of Brooks and Jepson that venous obstruction is the chief causative factor in the production of Volkman's ischemia. The pressure causing the obstruction may come from without (splints or bandages of a too flexed elbow) or from within (unreduced displacement of bones and subfascial hematoma). It is Jones' opinion that ischemic contracture might occur in spite of every precaution, but nevertheless the best treatment is prevention. The prophylactic measures which he advises and which have been successful in preventing the development of any instance of ischemia in his own practice are the following:

1. Reduction of dislocations and displaced bones as soon as possible. He does not advocate leaving unreduced a supracondylar fracture for several days in order to avoid ischemia. His method of reduction has been as follows: "I first extend the arm, supinating and pulling it at the same time. While the thumb is placed on the upper fragment the extended and stretched elbow should be flexed. This usually and without difficulty gives a complete reduction."

24. Albee, Fred H.: *Myofascitis from Orthopedic Standpoint*, J. A. M. A. 91:1364 (Nov. 3) 1928.

25. Jones, Robert: *Brit. M. J.* 2:639 (Oct. 13) 1928.

2. Using no force in flexing the elbow. No force should be necessary; if the arm does not flex easily, it is suggestive of blocking due to displaced fragments.

3. Avoidance of circular compression.

4. Avoidance of all splints.

The wrist is slung in a collar and cuff sling under the chin. Whether or not there is swelling, it is a mistake to bandage the arm to the forearm or the elbow to the side.

5. For the first few days, critical observation of all fractures about the elbow.

For treatment of the fully developed condition, the author has for years used nothing but his own previously described method of gradual stretching, and he has often obtained good results by this method in patients who had been subjected to operation previously without success. In his experience, operative treatment has not been helpful; and he warns against bone resections, tenoplasties, myotomies and tenotomies.

[ED. NOTE.—Robert Jones first wrote on Volkmann's ischemic paralysis in 1908. Now, twenty years later, he has given his present views on the subject in a brief paper. No abstract can do justice to this paper, in which every conclusion and suggestion are based on a lifetime of experience.]

Bailey²⁶ stated that he has transplanted the internal epicondyle of the humerus by suturing it into a subperiosteal bed one third of the way down the shaft of the ulna for the relief of Volkmann's ischemia. Three weeks after the operation, the fingers could be completely extended. At the end of seven months, the patient had recovered almost perfect function in the limb. The operation was performed four months after the onset of the ischemia, which followed a supracondylar fracture. Massage and splintage had been tried in the interval, without any appreciable improvement.

Spontaneous Dislocations of Hip Joint During Early Life.—Hart²⁷ analyzed twenty-eight cases of spontaneous dislocation of the hip in children. He found that sixteen followed a metastatic septic arthritis, four were due to poliomyelitis, four to spastic paralysis and four resulted from tuberculosis and chronic arthritis. He considered that the essential factor in all cases is a muscular imbalance. Prevention is the best form of treatment, and to this end it is necessary to keep the hip from assuming the adducted, flexed and inwardly rotated position. Constant traction, if properly applied, is an effective therapeutic measure.

26. Bailey, Hamilton: Brit. J. Surg. 16:335 (Oct.) 1928.

27. Hart, V. L.: Spontaneous Dislocations of Hip Joint During Early Life, Arch. Surg. 17:587 (Oct.) 1928.

"*Riders' Leg.*"—Writing of "riders' leg," Winn²⁸ stated that he has encountered forty-two cases of this injury at the Cavalry school during the past two years. It is of great economic importance, being one of the chief causes of inability to ride among officers. "Riders' leg" is rare among enlisted men who use the McClennan type of saddle with long stirrups. The officers use a flat saddle with short stirrups. The cause is a severe strain of the adductor muscle group. The muscles involved are the pectineus, adductor brevis, adductor longus and adductor magnus. The author has never been able to demonstrate gross periosteal evulsion. The injury in all cases observed followed sudden exertion of the muscles due to an unexpected movement of the horse. The symptoms are sudden severe pain in the thigh, gradually becoming so severe that further riding is impossible. Pain recurs with attempted adduction or on walking with a long stride. Acute tenderness is found over the upper portion of the adductor longus. In some cases, ecchymosis is noticed in the pubic region. In most instances, recovery takes place in from a few days to two weeks. The injury, however, predisposes to further strains of the adductors. In recurrent cases, several months are sometimes required for recovery. Treatment consists in rest and the application of heat in mild cases. A diagonal cross hatched strapping with adhesive plaster from close up in the crotch to the midthigh gives immediate relief in mild cases. In old recurrent cases, the author uses an elastic thigh stocking.

SURGICAL PROCEDURES ON THE BONES, JOINTS AND TENDONS

Operative Lengthening of the Femur.—Abbott and Crego²⁹ described a method of lengthening the femur in patients with unilateral shortening of the leg which they have used successfully in eight patients. The same principle was employed as in their method of lengthening the tibia and fibula previously described. After performing a Z shaped osteotomy of the shaft of the femur and inserting transfixion pins in the upper and lower ends of the bone, an apparatus is applied which permits gradual distraction of the fragments while maintaining accurate alinement. By employing this apparatus, the authors were able to obtain an average increase in length of $2\frac{1}{2}$ inches in four weeks. The lengthening finally obtained varied from $1\frac{1}{2}$ to $3\frac{1}{2}$ inches. There were no infections and no nonunions. The authors do not recommend this as a routine procedure, but advocate it in carefully selected cases.

[ED. NOTE.—Abbott and Crego's careful work and ingenious apparatus have made lengthening of the lower extremity a dependable procedure. About sixty patients have been operated on by them, with

28. Winn, D. F.: Mil. Surgeon **63**:507 (Oct.) 1928.

29. Abbott, L. C., and Crego, C. H.: South. M. J. **21**:823 (Oct.) 1928.

uniform success. There have been no disasters. At present, lengthening of the tibia and fibula is more of a standardized procedure and involves fewer difficulties than lengthening of the femur, but the latter method is still being developed.]

Results of Stabilizing Operation for Paralytic Hips.—Dickson³⁰ made a further report on the results obtained by the operative method previously described by him for stabilizing hips rendered unstable by paralysis of the gluteus maximus and minimus muscles. The operation consists in transplanting the origin of the tensor fasciae femoris from its position just external to the anterior superior spine to a new position on the crest of the ilium in the vicinity of the posterior superior spine, thus bringing the muscle posterior to the axis of the hip joint where it acts as an extensor instead of a flexor of the hip.

Dickson has operated on forty-six patients. Of these, thirty-two have been under observation a sufficiently long time to permit an estimation of the final result. In ten of these, the limp has been eliminated or greatly improved; in fourteen there has occurred a definite improvement in stability of the hip, but with a definite limp still remaining; in eight, the results have been failures in that no more improvement has been obtained than could have been expected by overcoming the hip-joint flexion deformity which was present. All the failures were in cases in which a weak or paralyzed tensor fasciae femoris muscle was used.

Operative Fusion for Tuberculosis of the Spine.—Henderson³¹ discussed the rôle of fusion operations of the spine in Pott's disease, basing his remarks on a study of 301 patients on whom this operation in one of its various forms had been performed at the Mayo Clinic between 1912 and 1925. Albee's bone graft technic was employed in 269 patients and Hibbs' osteoplastic method in 32. In a few instances after the Albee method, secondary operations were required because of fracture of the graft. Only 16 of the patients operated on were under 10 years of age, and 227 of the patients were between 20 and 40 years of age.

It was found that the length of time necessary to complete the convalescence was nearer two years than one and sometimes more, and that the patients who were able to rest and observe the general anti-tuberculous regimen improved much faster than those who did not. The author concluded that the operation has an important rôle in helping to obtain a cure and that it ought to be employed in adult patients who are in good general condition, and if there is no evidence of

30. Dickson, Frank D.: J. Bone & Joint Surg. **10**:712 (Oct.) 1928.

31. Henderson, M. S.: Operative Fusion for Tuberculosis of Spine, J. A. M. A. **92**:45 (Jan. 5) 1929.

impending wide dissemination of the disease and no draining sinuses to contaminate the operative field. He expressed the conviction that it is useless to subject to this operation patients who in addition to Pott's disease have advanced tuberculosis of the lungs or of the genito-urinary tract.

Extra-Articular Fusion of the Tuberculous Hip in Children.—Stating his conviction that patients with tuberculosis of the hip never recover a useful degree of motion, Kidner³² advocated fusion of the hip by the extra-articular method. He considered this to be indicated even in the case of children. He has performed this operation in sixteen children and has followed them through to the end-result stage. In all cases, the progress of the disease has been arrested and symptoms relieved. He considers the juxta-articular methods of Kappis and Hibbs and the free graft method which he has devised preferable to the para-articular methods of Albee, Calvé and others. From this study he concluded that the earlier in the disease the operation is performed, the less will be the shortening and the shorter the period of invalidism.

[ED. NOTE.—We have advocated arthrodesis for tuberculosis of the hip in adults for a number of years, but have been reluctant until recently to take the same stand in respect to children and to abandon all hope of recovery without ankylosis. Subsequent experience has, however, finally convinced us that to delay operation is to expose the child to serious risks and that ankylosis in good position is not only the best guarantee of cure, but also the best means of preserving maximum function.]

Recurrent Dislocation of the Shoulders.—Oudard³³ described a new operative procedure for the relief of recurring dislocation of the shoulder which in his hands has yielded satisfactory results. Its aim was to prevent the head from leaving the glenoid by the restraining influence of a bone block. Briefly, the operation consisted in exposing the front of the shoulder by turning back the anterior border of the deltoid, splitting the coracoid process in its long axis and detaching the outer half with its muscular insertions, and dividing the subscapularis muscle and the anterior portion of the capsule. The edges of the capsule and the subscapularis muscle were then overlapped and sutured in order to reef the relaxed structures. Finally, the detached portion of the coracoid was brought up into position and its base fixed by wire to the tip of the remaining portion. This resulted in the coracoid process being prolonged a distance of about 3 cm., sufficient for it to act as a bone block preventing the humeral head from displacing anteriorly.

32. Kidner, F. C.: End-Results of Extra-Articular Fixation of Tuberculous Hip in Children, J. A. M. A. **91**:1865 (Dec. 15) 1928.

33. Oudard: Presse méd. **36**:201 (Feb. 15) 1928.

[ED. NOTE.—It has been reliably stated that more than 150 different operative procedures have been devised for overcoming recurrent dislocation of the shoulder. Analysis of these different operations shows that with a few exceptions they fall into three groups: first, those dealing with the capsule and employing some method of strengthening it such as reefing, overlapping, etc.; second, those dealing with the humeral head and employing some adventitious tissue to hold it in place, fixation with fascia or tendon or transplantation of muscle, and, third, those which deal with the glenoid, aiming to prevent displacement by the introduction of a bone block. All of these methods have proved effective, and the criterion for selection should be simplicity as well as reliability. Fixation of the humeral head by the use of fascia or tendon seems to have a considerable advantage in this respect.]

Tendon Transplantation Technic.—In operations for the transplantation of tendons, Royle³⁴ recommended using the transplanted tendon as a living suture. He did this by splitting off strips from the transplanted tendon, threading them on fascial suture needles and weaving them in and out of the paralyzed tendon to which the transplant is to be secured.

FRACTURES

Fractures of Metatarsals and Phalanges.—Magnuson³⁵ found from his own experience that fractures of the metacarpals and phalanges were capable of producing disability far in excess of their apparent importance because of their effect on the function of the hand. Unless the fracture is properly reduced and the fragments maintained in correct alinement, the injury results almost uniformly in stiffness of the fingers and constitutes a serious handicap.

In fractures of the metacarpal bones, it is the pull of the interossei that has to be resisted with its tendency to cause a dorsal bowing or angulation of the fragments. In fractures of the middle phalanges of the fingers, the lumbricales muscles exert an extensor action on the distal fragments while the interossei tend to flex the proximal fragment causing the forward bowing deformity which presses against the flexor tendon of the finger.

[ED. NOTE.—Fractures of the phalanges and metacarpals are serious injuries and in our experience, yield a large degree of disability. The results are bad when the fractures are not properly reduced and are far from good even when anatomic reposition is obtained. Splinting should be reduced to a minimal period and motion started as early as possible if the results are to be improved.]

34. Royle, N. D.: J. Coll. Surgeons, Australasia 1:115 (July) 1928.

35. Magnuson, Paul B.: Fractures of Metacarpals and Phalanges, J. A. M. A. 91:1339 (Nov. 3) 1928.

Compression Fractures of the Spine.—In a general survey of fractures of the spine, Osgood³⁶ found that compression fractures represent more than 50 per cent and that of these from 70 to 80 per cent involved the eleventh and twelfth dorsal or the first and second lumbar vertebrae. Most of them resulted from hyperflexion injuries. In untreated patients, one encounters the three stages of disability described by Kummell: first, the stage of initial injury; second, a period of comparative well being, and third, development of kyphos and pain. As far as diagnosis is concerned, the important thing is to suspect such an injury. Discussing the treatment in the different types of fracture, Osgood stated that fractures of the sacrum or coccyx usually respond to rest; that fractures of a single vertebra do well if the patient is treated in the recumbent position for from six to eight weeks with the aid of plaster jackets or hyperextension frames; that long standing cases, in which treatment has not been given, with persistent pain and deformity should be given the benefit of a fusion operation, which, however, should be preceded by a course of postural and corrective treatment.

Fractures of the Neck of the Femur in Childhood.—From a review of the literature, Colonna³⁷ concluded that fracture of the neck of the femur is an unusual injury in childhood. He reported six instances of this injury in children, the ages ranging from 5 to 16 years. The fractures were caused by severe violence. The symptoms were less severe than in adults, and there was only moderate disability. One of the patients was treated for a contusion of the knee for several weeks. Five of the fractures involved the cervicotrochanteric region, three being incomplete and two complete, and one was situated in the narrow portion of the neck. Five of the six patients were treated by a spica with the hip in abduction and one was treated with the hip in abduction in a Bryant frame. Three of the patients recovered with perfect function; in one, the limb was $\frac{1}{8}$ inch shorter but no limp or limitation of motion was present. One, with an incomplete cervicotrochanteric fracture, showed $1\frac{3}{4}$ inches shortening and marked limitation of motion, but was able to get about without any apparatus, and the last had $\frac{1}{4}$ inch shortening with slight limitation in abduction.

DISLOCATIONS

Apparatus for Reduction of Fracture Dislocations of the Cervical Spine.—King³⁸ described a method of reduction for fracture dislocations of the cervical spine which have proved useful in his hands.

36. Osgood, R. B.: New England J. Med. **199**:861 (Nov. 1) 1928.

37. Colonna, P. C.: Ann. Surg. **88**:902 (Nov.) 1928.

38. King, J. E. J.: Am. J. Surg. **5**:507 (Nov.) 1928.

A plaster cast was applied encircling the body, and in it was incorporated an apparatus consisting of two steel shoulder pieces mounted on which were two steel uprights terminating in a cross bar. A halter was fitted to the patient's head, and this in turn was connected with the cross bar. By means of a ratchet gear traction was exerted in the line of deformity until reduction was accomplished. This apparatus was worn for a period of six or eight weeks when a Thomas collar was applied.

Intra-Articular Dislocation of the Patella.—Jones³⁹ described an unusual injury to the patella in a boy, aged 11, following a fall. The patella was rotated 90 degrees so that the upper edge was directed backward and became wedged in the intercondylar notch of the femur. Manipulation under anesthesia failed to reduce the dislocation. At operation the knee joint was opened, and the bone forcibly levered back into position; it was then necessary only to suture the incision in the joint capsule made by the operator. The quadriceps extensor insertion had been stripped off the upper and anterior surfaces of the bone, but was not ruptured. Seven weeks after the accident, the knee joint was normal. Jones stated that fourteen similar cases have been described.

AMPUTATIONS

An Operation for Making the Forearm Prehensile after the Loss of a Hand.—Henry⁴⁰ succeeded in providing a patient whose left forearm had been amputated at the wrist with a prehensile extremity by splitting off a rod of bone from the outer side of the radius and enveloping this, together with the muscles in contact with it (flexor carpi ulnaris, flexor longus pollicis, radial wrist extensors, dorsal tendons of the thumb and the brachioradialis) and the radial artery, with skin. Active pronation of the forearm brought this newly formed digit into opposition with a fixed digit, supplied by means of a prosthesis. The patient was subsequently able to write with the left forearm. Henry expressed the belief that he could have dispensed with the prosthesis if he had partially fractured the ulna and bent it so as to give the newly formed digit a living opponent.

OSSIFICATION OF EXPERIMENTAL FRACTURES

Ossification After Fractures.—Ravdin and Morrison,⁴¹ in a series of dogs, fractured the radius by open operation and studied the rate of ossification under various experimental conditions. The animals

39. Jones, Percy J.: Brit. J. Surg. **16**:338 (Oct.) 1928.

40. Henry, Arnold K.: Brit. J. Surg. **16**:188 (Oct.) 1928.

41. Ravdin, I. S., and Morrison, M. E.: Ossification After Fracture. Arch. Surg. **17**:813 (Nov.) 1928.

were divided into four groups: those in the first group were given 20 cc. of cod liver oil daily; those in the second group were given parathyroid extract Collip to raise the serum calcium level; those in the third group were subjected to thyroparathyroidectomy to lower the serum calcium level of the blood, and the animals in the fourth group were used as controls.

From their study of the results, they were inclined to minimize the effect on normal bone of a deficient inorganic phosphorus and calcium serum content. Union occurred in every instance with the exception of two hypocalcemic animals which did not live long enough for ossification to occur.

EFFECT ON THEIR FUNCTION OF STRETCHING NERVE TRUNKS

Tests on Sciatic Nerves.—By applying various amounts of tension to the sciatic nerve of a cat, Forbes⁴² demonstrated that the power of conduction of an impulse is much impaired. Even the slight amount of tension necessary to dissect out the nerve is sufficient to affect its power of conduction considerably. Tension applied to a frog's nerve, however, has much less effect than in the mammal. The mammalian nerve undergoes a recovery period after stretching; presumably a nerve with intact blood supply would recover much more rapidly.

42. Forbes, A.: New England J. Med. **199**:555 (Sept. 20) 1928

CORRELATIONS OF INTERNAL AND EXTERNAL PANCREATIC SECRETION

I. GENERAL CONSIDERATIONS AND REVIEW OF THE LITERATURE *

G. DE TAKATS, M.D.†

CHICAGO

The relationship of the various structural elements of the pancreas has intrigued many investigators. Laguesse¹ evolved a remarkable theory of "balancement," maintaining that acini are continuously transforming into islands and that these two structures hold each other in a balance according to functional needs. A large series of experiments was conducted after the discovery of the islands to see what would happen to the islands when the external secretion was obstructed. The literature up to 1909 is summarized in Moldenhauer's inaugural dissertation;² the more recent studies have been discussed critically in Herxheimer's monograph.³ One group of investigators firmly believes in a limiting membrane and a complete independence of the islands from the rest of the pancreas. A large number of investigators claim possible transitions of acini into insular epithelium. Another small but authoritative group of investigators concedes the proliferation and transformation of duct epithelium into islands when the duct no longer excretes.⁴

A study of the development of the islands led to the uniform result that the islands originate in small buds of the duct epithelium and can be recognized as early as in the embryo⁵ of 80 mm. Here again, how-

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1. Laguesse, F.: *Preuves experimentales du balancement dans les ilots endocrinologiques du pigeon*, *Compt. rend. Soc. de biol.* **67**:94, 1909; *Preuves experimentales du balancement dans les ilots endocrinologiques du pancreas*, *J. de physiol. et de path. gén.* **13**:1, 1911.

2. Moldenhauer, Johannes: *Ueber das Verhalten des Pankreas, insbesondere der Langerhanschen Zellinseln nach Gangunterbindungen*, Inaug. Diss., University of Bern, Wiesbaden, R. Bechtold & Company, 1909.

3. Herxheimer, G.: *Pankreas*, in Hirsch, M.: *Handbuch der inneren Secretion*, Leipzig, Curt Kabitzsch, 1927, vol. 1.

4. Otani, Sadao: *Studies on the Islands of Langerhans in Human Pancreas*, *Am. J. Path.* **3**:1 and 123, 1927.

5. Weichselbaum, S., and Kyrle: *Ueber das Verhalten der Langerhans Inseln des menschlichen Pankreas im fötalen und postfötalen Leben*, *Arch. f. mikr. Anat.* **74**:223, 1909.

ever, some authors deny any relationship between glandular parenchyma and islands⁶ whereas another group claims direct transitions from acini to islet tissue.⁷

The comparatively large amount of islet tissue in the fetal pancreas has been emphasized by two recent exhaustive studies of the embryology of the islands.⁸ The maximal number occurs between the twenty-sixth and the thirty-second week. The number of islands then slowly diminishes up to birth, rapidly during the first postfetal year, and then again more slowly to the fourth year, after which their number remains fairly constant.

The observations on the pancreas of congenitally syphilitic children are interesting. The great increase in interstitial connective tissue prohibits the development of the glandular element, and a large number of small ducts and islands are visible. The appearance of the pancreas of a syphilitic new-born infant corresponds to a stage seen normally around from the seventeenth to the eighteenth week.⁹

The observations in pathologic processes of the pancreas, when a gradual obstruction of the external secretion has taken place, would indicate that not infrequently hypertrophy and hyperplasia of the islands occurred. In Koch's case¹⁰ a marked increase of islands was found in spite of the fact that the entire gland had turned into an infiltrating scirrhus. That changes in sugar tolerance are frequently absent in carcinoma of the pancreas and chronic pancreatitis is generally admitted.¹¹

In experimental ligation of the duct in the fetal pancreas in pancreatic cirrhosis and in carcinoma of the head of the pancreas there is one common feature: namely, the gland does not function as a gland of external secretion. The question arises whether or not the reversion of the gland to a stage of inner secretion alone might cause a preponderance of this part of the glandular function. Mansfeld¹² pointed

6. Nakamura, Nobu: Untersuchungen ueber das Pankreas bei Föten, Neugeborenen, Kindern und im Pubertätsalter, *Virchows Arch. f. path. Anat.* **253**:286, 1924.

7. Seyfarth, F.: Neue Beiträge zur Kenntnis der Langerhansschen Inseln im menschlichen Pankreas, Jena, Gustav Fischer, 1920.

8. Nakamura (footnote 6). Seyfarth (footnote 7).

9. Herxheimer (footnote 3). Seyfarth (footnote 7).

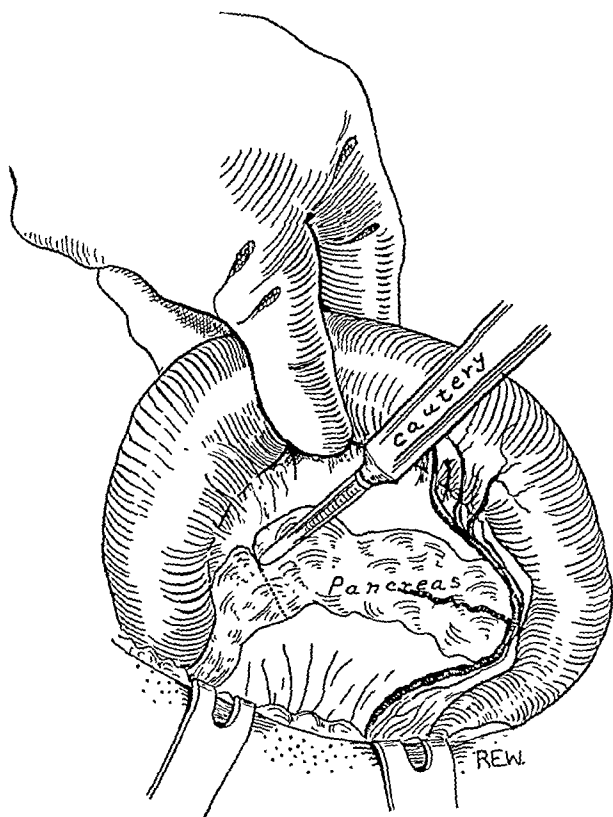
10. Koch, F.: Ein Adenom aus Inselzellen im Pankreas eines Nichtdiabetikers, *Virchows Arch. f. path. Anat.* **216**:25, 1914.

11. Gross, O., and Guleke, N.: *Die Erkrankungen des Pankreas*, Berlin, Julius Springer, 1924.

12. Mansfeld, G., and Szirtes, L.: Ueber die Beziehungen zwischen äusseren und inneren Secretion der Drüsen, *Arch. f. exper. Path. u. Pharmacol.* **130**:1 and 28, 1928.

out that possibly analogous conditions occur in the testis when the vas is ligated and in the parotid when Stenson's duct is tied. The thyroid gland possesses a duct at one time during development. The thyroid in the tunicates and in the amphioxus secretes a sticky material. In the higher vertebrates the internal secretion develops seemingly at the expense of the external secretion.

There is one condition that might possibly stimulate inner secretion of the pancreas, namely, the increased functional demand for such a



Division of the tail of the gland with electric cautery.

secretion. The islands do become larger in partially pancreatectomized animals,¹³ and the pancreas of the diabetic person shows adequate proof of compensatory attempts.⁹

This study was undertaken for the purpose of examining the effect of isolation of the tail of the pancreas on its insular activity. While the external secretion could flow undisturbed into the duodenum, the tail would be converted into a ductless gland. Such a procedure was

13. Allen, F. M.: *Glycosuria and Diabetes*, Boston, W. M. Leonard, 1913.

suggested by Mansfeld,¹⁴ who claimed an increase in sugar tolerance following such a procedure in the dog, lasting as long as three years. Alpern and Leites¹⁵ confirmed his results in a short preliminary report. Nather, Priesel and Wagner,¹⁶ who first confirmed Mansfeld's results, reported in a second paper that the increased tolerance is only temporary. Wohlgemuth¹⁷ found a decreased sugar tolerance following ligations of the duct and believed it to be the result of a chronic sympathicotonia with increased response to epinephrine.

This work was undertaken to study the histologic changes in the pancreas following the separation of the tail from the rest of the gland. In a second paper, the changes in sugar tolerance will be discussed, while other papers will deal with associated effects produced by partial pancreatic obstruction.

14. Mansfeld, G.: *Versuche zu einer chirurgischen Behandlung des Diabetes*, Klin. Wchnschr. **3**:2378, 1924; *Versuche zu einer operativen Behandlung des Diabetes*, *ibid.* **6**:105, 1927; footnote 12.

15. Alpern, D., and Leites, S.: *Ueber den Einfluss der Unterbindung des ductus pankreaticus auf den Blutzucker*, Klin. Wchnschr. **4**:1551, 1925.

16. Nather, K.; Priesel, R., and Wagner, R.: *Die Beeinflussung der Blutzuckerspiegels durch Unterbindung der Ausführungsgänge der Bauchspeicheldrüse beim Hund*, Klin. Wchnschr. **5**:932, 1926; *ibid.* **6**:2089, 1927.

17. Wohlgemuth, Julius, and Mochizuki, N.: *Ueber das Verhalten des Blutzuckers beim Kaninchen unter verschiedenen Bedingungen und ueber seine Verteilung im Blut*, Biochem. Ztschr. **150**:123, 1929. Wohlgemuth, J., and Seo, T.: *Ueber experimentelle Erzeugung von chronischer Sympatricotomie beim Kaninchen*, Biochem. Ztschr. **164**:271, 1925.

CORRELATIONS OF INTERNAL AND EXTERNAL PANCREATIC SECRETION

II. THE HISTOLOGIC CHANGES IN THE ISOLATED TAIL OF THE PANCREAS *

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CHICAGO

The purpose in this study was to examine the three main structural elements of the pancreas—acini, ducts and islands—after a part of this gland had been excluded from external secretion. It must be emphasized that this procedure is not identical with ligation of the duct, which method has been used to a great extent experimentally.¹ The exclusion of pancreatic juice from the intestines results in serious nutritional disturbances and may influence the inner secretion of the pancreas. Ligation of the tail of the pancreas, as suggested by Mansfeld,² leaves a sufficient part of the gland to secrete ferments and turns only ductless that part of the gland which is known to contain comparatively more islet tissue.

Recent studies by Ukai,³ Herxheimer and Carpenter⁴ and Jorns⁵ uniformly state that a sclerosis of the pancreas takes place following ligation of the duct. The islands, however, resist this process, and may even increase in size. They even survive transplantation⁶ for a long time. Special stains have been employed by some workers to identify the remaining structures as islet tissue.⁷ A systematic examination of

* Submitted for publication, April 29, 1929.

† Elizabeth Ward Fellow in Surgery.

1. Moldenhauer, Johannes: Ueber das Verhalten des Pankreas, ins besondere der Langerhansschen Zellinseln nach Gangunterbindungen, Inaug. Diss., University of Bern, Wiesbaden, R. Bechtold & Company, 1909. Herxheimer, G.: Pankreas, in Hirsch, M.: Handbuch der innern Secretion, Leipzig, Curt Kabitzsch, 1927, vol. 1.

2. Mansfeld, G., and Szirtes, L.: Ueber die Beziehungen zwischen äusseren und inneren Secretion der Drüsen, Arch. f. exper. Path. u. Pharmacol. **130**:1 and 28, 1928. Mansfeld, G.: Versuche zu einer chirurgischen Behandlung des Diabetes, Klin. Wchnschr. **3**: 2378, 1924; Versuche zu einer operativen Behandlung des Diabetes, *ibid.* **6**:105, 1927.

3. Ukai, L.: Morphologisch-biologische Pankreasstudien, Mitt. ü. allg. Pathol. u. path. Anat. **3**:1, 1927.

4. Herxheimer, G., and Carpenter, E.: Ueber das Verhalten der Langerhansschen Zellinseln des Pankreas und die Insulinbildung nach Gangunterbindung, Beitr. z. path. Anat. u. z. allg. Pathol. **76**:270, 1927.

5. Jorns, G.: Die Sklerose des Pankreas nach Unterbindung des Ausführungsganges und die Transplantation des sclerotischen Gewebes, Beitr. z. klin. Chir. **139**:325, 1927.

6. Ukai (footnote 3). Jorns (footnote 5).

7. Kirkbride, M. B.: The Islands of Langerhans After Ligation of the Pancreatic Ducts, J. Exper. Med. **15**:101, 1913. Ukai (footnote 3).

the separated tail at various intervals to study the degenerative and regenerative processes of the pancreas was undertaken to serve as a basis for further studies.

METHOD OF EXPERIMENTATION

Healthy dogs weighing from 10 to 15 Kg. were used. The operation was performed with the animals under ether anesthesia after a preliminary injection of morphine, $\frac{1}{4}$ grain (16 mg.), and atropine, $\frac{1}{60}$ grain (1 mg.). Through a small midline incision the index finger of the left hand palpated the pylorus and delivered the mobile duodenum into the wound. This brought the pancreas into the field. At the point where the tail of the pancreas borders the fixed part of the gland, a massive ligature was thrown around the gland. In later experiments the gland was cut between the two ligatures, or simply cut and the individual bleeders tied. In the last six cases the gland was cut with the electric cautery.* This made the use of a ligature unnecessary. The absence of foreign material, thereby lessening the tissue reaction around the ligatures, was thought to be of some importance.

Sections were taken for histologic study at various intervals from the isolated and undisturbed portion of the gland. Ten of the twenty-five dogs used in this series lived a year or longer, whereas eighteen could be observed for at least six months. They were on the standard diet, and lost weight during the first few weeks, but maintained their weight later and seemed in good condition. Occasional blood counts revealed no kennel anemia. The removed specimens were fixed in a diluted solution of formaldehyde, U. S. P. (10:1) and stained with hematoxylin and eosin. Later, the neutral formol-Zenker fixation was used, and Bensley's special stains were employed.

SUMMARY OF HISTOLOGIC OBSERVATIONS

Two days following separation of the tail, the dominating impression was that of edema. The tail was soft and friable and was markedly swollen. The small ducts were dilated, and the acini were markedly distended with stagnant secretion. Their epithelium was flattened. The nuclei did not stain well, were irregular and had a hazy contour. The islands seemed swollen, but generally were intact (three specimens).

Two weeks following separation of the tail, the tail looked anemic and grayish white. Its consistency was hard and nodular, similar to that found in chronic pancreatitis of man. Under the microscope, the individual lobules were compressed and separated from each other by a moderate increase of connective tissue. This concentric, intralobular fibrosis caused the remaining parenchyma to stand out clearly. The acini still maintained their form, but the individual cells had partly undergone degeneration. The protoplasm consisted of numerous vacuoles; the nucleus was fragmented and pyknotic. The zymogen granules stained poorly. The small ducts were dilated; their epithelium showed infolding

8. Prof. W. T. Bovie and his staff of the department of biophysics have given their utmost cooperation. Dr. Bovie's newest model of high frequency apparatus was used (Surg. Gynec. Obst. 47:751, 1928).

at certain places. There was marked mitotic activity. The islands seemed well preserved and showed no evidence of degeneration. In the sclerotic gland with compressed acini, they stood out clearly. There was no evidence of any activity on their part (three specimens) (fig. 2).

Four weeks following separation of the tail, the tail was even more sclerotic. It had turned into a whitish, narrow cord. Its consistency was hard and granular. There was more connective tissue than in the previous specimen, and not only interlobular but intralobular strands of fibrous tissue were seen. An increase in fatty tissue could also be observed. The acini were hardly recognizable, except as irregular masses

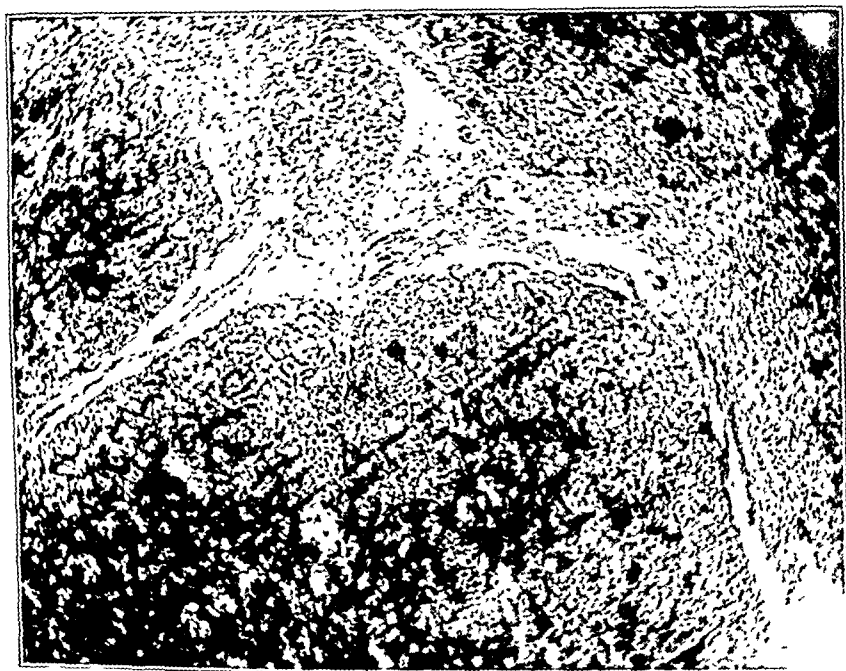


Fig. 1.—Two weeks following ligation of the tail. There is a moderate amount of perilobular sclerosis. The edema is most marked in the connective septums, but the islands are also swollen; low power.

of detritus into which connective tissue proliferated. The ducts were not dilated markedly; their wall was thick. Mitotic activity and occasional buds and infolding of the epithelium could be observed frequently. The islands did not seem increased in size or number. They stained well, but showed a certain diffuse hyaline-like structure in their center. There was no mitotic activity (two specimens) (fig. 2).

Six weeks following the separation, the tail was completely cirrhotic. Under the microscope, a dense connective tissue had taken the place of the lobules. Acinar structures could not be recognized. There was a marked proliferation of the minute ducts, which spread lengthwise and

crosswise over the field. Their epithelium was in a stage of mitotic activity. Occasionally, small buds, papillary folds and cystic dilatations could be found. The islands were still preserved, but were not particularly large or numerous except in one specimen, in which they stood out in large numbers. They did not show mitotic activity (three specimens) (figs. 3 and 4).

After twelve weeks, the microscopic appearance of the ligated tail was that of a whitish-gray firm cord. Histologically, the lobules had been compressed to small irregular structures. The connective tissue had proliferated into these lobules. The larger ducts were dilated, but

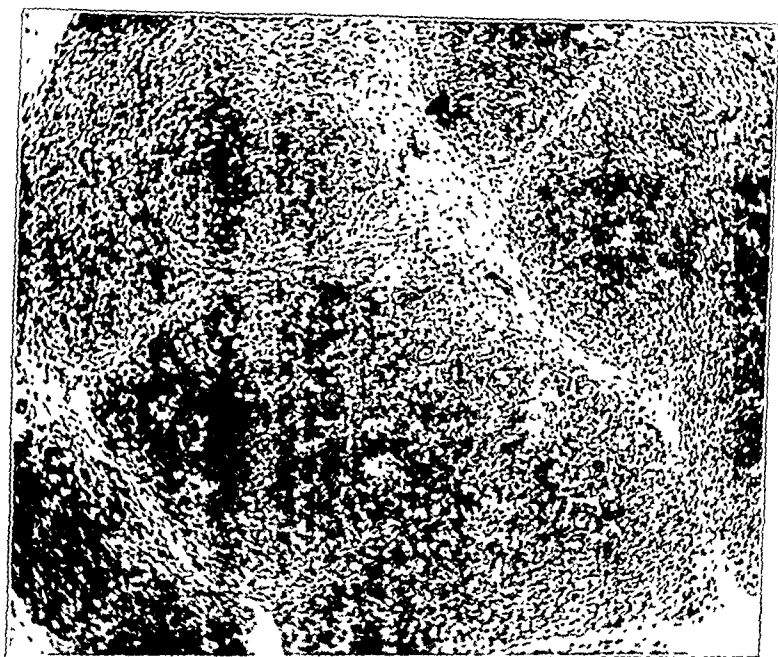


Fig. 2.—Four weeks following ligation. There is a marked increase of connective tissue, not only around but in the lobules. The acini are shrunk, and their cell nuclei are pyknotic. The islands are well preserved and fairly numerous; low power.

a few minute ducts were visible. The islands were numerous, and were not only well preserved, but larger in diameter. They showed mitotic activity. On one slide, in which the tail had been separated by the high frequency current, there was much less fibrosis, and the acinar structure was well preserved. The islands were numerous on the slide, and the number of capillaries around the islands was striking. This whole slide was characterized by a lack of fibrosis, but a large number of dilated capillaries was seen. The epithelium of the ducts was columnar with frequent mitoses and infolding. There was a mass of desquamated epithelium in the lumen (figs. 5 and 6).

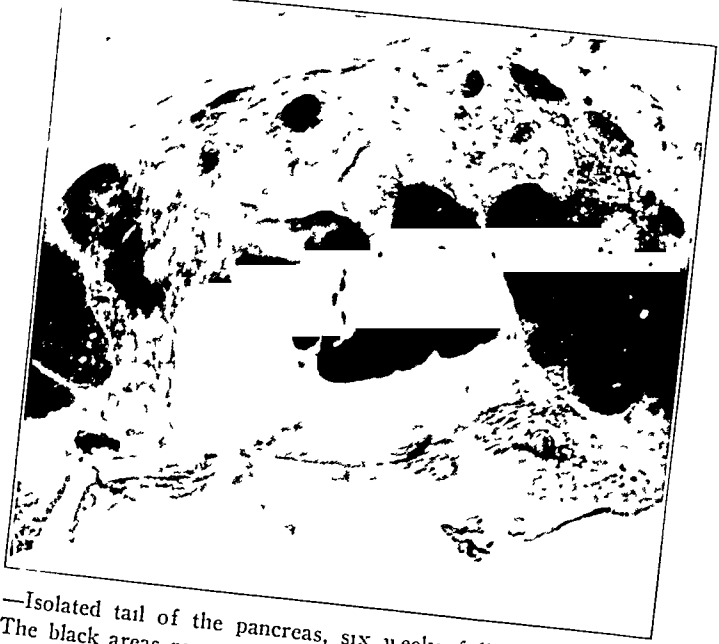


Fig 3—Isolated tail of the pancreas, six weeks following division with the cautery. The black areas represent glandular parenchyma staining red with acid fuchsin-methyl green stain. The fibrosis is fairly marked in the upper half of the section. The main duct is seen markedly dilated.

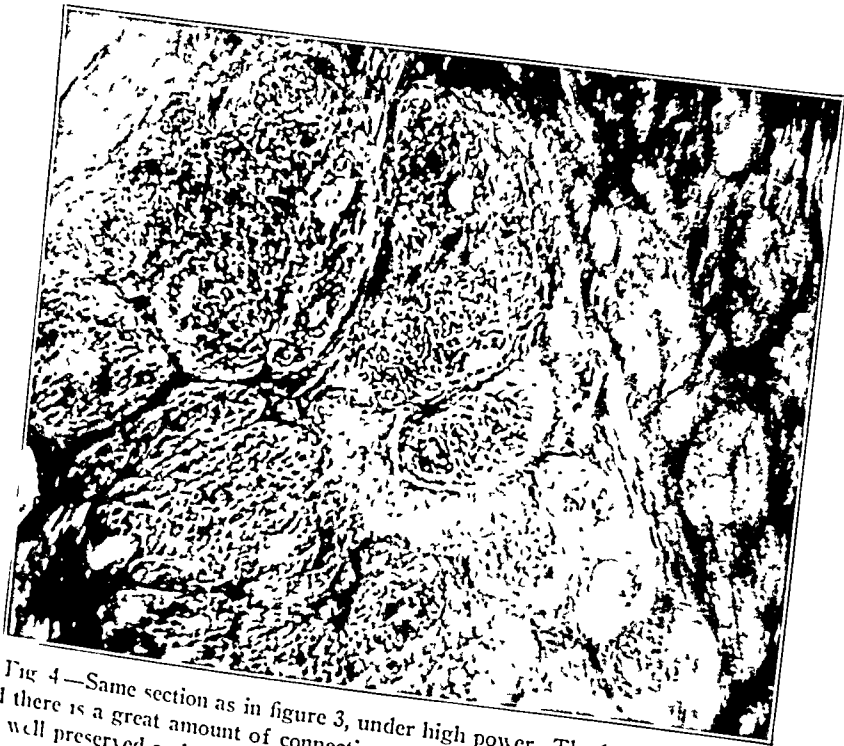


Fig 4—Same section as in figure 3, under high power. The lobuli are shrunken, and there is a great amount of connective tissue between the lobules. The islands are well preserved and are not involved in the sclerotic process.

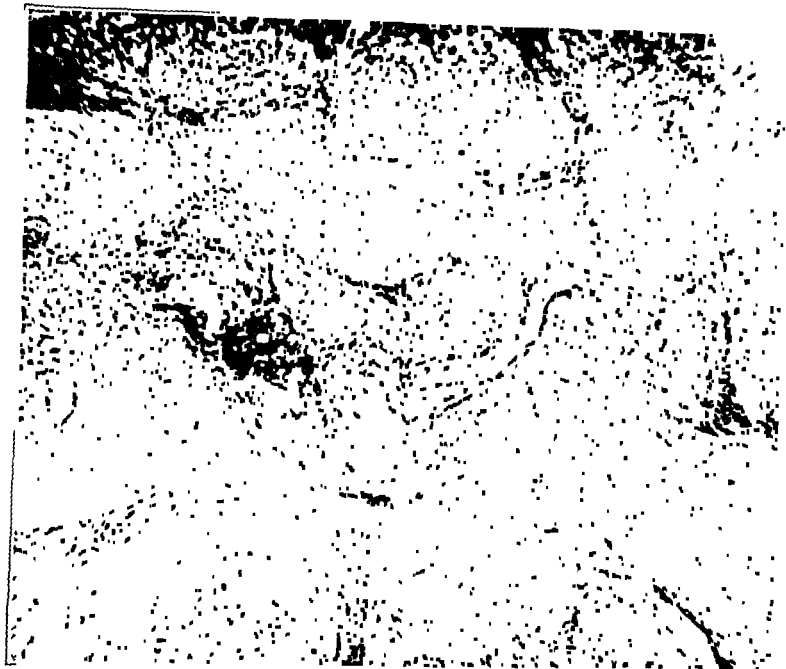


Fig. 5.—Twelve weeks following the isolation of the tail. There is a diffuse sclerosis of the gland. There are numerous small and minute ducts embedded in the sclerotic tissue. The epithelium of the ducts is high and shows infolding.

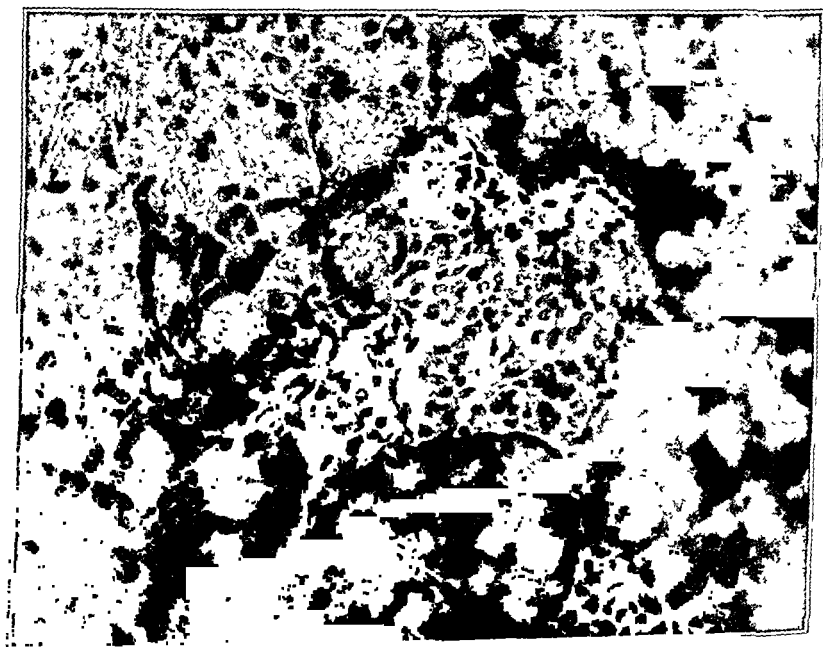


Fig. 6.—Same section as in figure 5, under high magnification, showing a well preserved island of considerable size. Below it is connected with another island which is probably the same island but hardly connected at the level of the section.

After sixteen weeks, the diffuse sclerosis with small remnants of acini dominated the field. The vessels had thick walls but were patent. The small ducts were numerous, and a large number of minute ducts was visible. Large masses of accumulated cells stood out in the connective tissue. Some of them were miliary abscesses. Others showed conglomerations of histiocytes and macrophages. There were epithelial cells with large light protoplasm which had the usual appearance of islet tissue. They were identified as such with special stains. These islets had a diameter of from three to thirty times the normal. In many



Fig. 7.—Sixteen weeks following ligation of the tail; there is complete absence of acini, and thickened but patent vessels. An intact ganglion is shown, and a large island appears in the left upper quadrant of the picture. There is no fibrosis within the island.

instances, they were grouped around a small duct with thickened walls (fig. 7).

After twenty-four weeks, no acinar elements could be detected in the sclerotic mass. Islet tissue was well preserved with typical capillary arrangement. The connective tissue was arranged in a wavy, circular configuration around the islands. In some places the solid epithelial masses seemed to be broken up by fibroblasts, and individual cells were visible. These nuclei seemed shrunk, and pyknotic (figs. 8 and 9). A transplant of a portion ligated twelve months previously had been made into the omentum. In the omental fat a large number of ducts

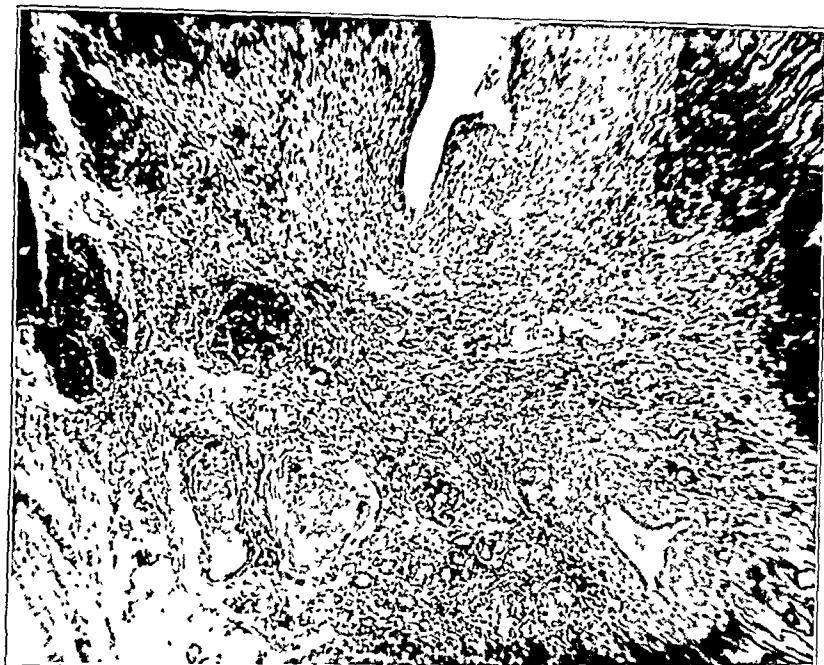


Fig. 8—Twenty-four weeks following ligation; there are a number of small newly regenerated ducts, similar to the regeneration of bile ducts in cirrhosis of the liver. There are remnants of lobules seen in the periphery of the picture. There are small areas of round cell infiltrations, plasma cells and histiocytes as a result of minute focal necroses.

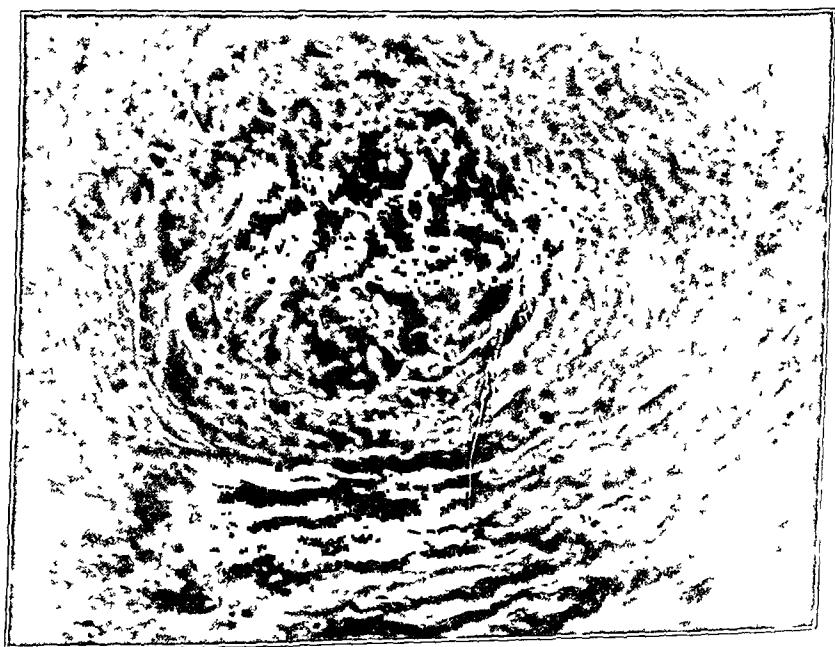


Fig. 9.—Twenty-four weeks following ligation. A large island, completely surrounded by insular waves of connective tissue, is seen. The island seems well preserved; the nuclei stain well.

with thick walls and high and frequently infolding epithelium were seen. Large structures of dendritic design, with light protoplasm and sharply staining nuclei were the only other cellular elements in the slides. These solid strands sometimes were drawn out to narrow cords. In other places, they formed round or oval structures with a lumen in the middle, as if they originated in ducts. Occasionally a small duct was found in the middle of these islands, with infolding epithelium. The transplant was well vascularized, a number of thick vessels surrounding the cellular elements in the omental fat. The sympathetic ganglions

Summary of Histologic Observations Following Isolation of the Tail of the Pancreas, with Four Additional Transplants into the Omentum

Postoperative Period, Days	Number of Specimens	Acini	Ducts	Islets	Ganglions	Connective Tissue
2	3	Distended	Dilated	Edematous	Edematous	General edema
14	3	Preserved	Epithelium active	Well pre- served	Well pre- served	Perilobular fibrosis
23	2	Poorly staining	Walls thick; infolding epithelium	Well pre- served	Well pre- served	Perilobular and intralob- ular fibrosis
42	3	Detritus	Desquam- ating epithelium	Numerous mitoses; well preserved	Well pre- served	Dense fibrosis
84	3	No acinar structure	Dilated; few minute ducts	Numerous; large diameters	Well pre- served	Very little fibrosis in the cauter- ized specimen
112	2	No acini plasma cells; histiocytes	Numerous minute ducts; buds	Large; mitoses	Well pre- served	Very dense fibrosis
168	2	No acini	Ducts less numerous	Partly in- vaded by fibrosis	Well pre- served	Intense sclerosis
210	2	No acini; fat	Occasional ducts	Well pre- served	Well pre- served	Intense sclerosis
330	1	Fat	Occasional ducts	Well pre- served; vascular	Well pre- served	Intense sclerosis
300 days; 160 days in omentum	4	Fat	Small ducts	Numerous	Well pre- served	Intense sclerosis

were also well preserved. The number of ducts was markedly decreased in contrast with slides from transplants of less duration. When they were seen, their epithelium was active, showed a number of mitoses and was cuboid or cylindric (figs. 10 and 11).

Five such transplants remained in the omentum for six months or more. They all showed the same picture. The longest time was 450 days, the shortest, 150. Briefly, they were all characterized by a complete absence of zymogenic cells and by a dense fibrous tissue, in which only two elements survived—small ducts and solid masses of large cells—which stained like islets. The capillary arrangement around such masses was also similar, if not identical, to that around the normal islets. The diameter of these solid cell complexes was from ten to thirty times that of the islets in the dog. Other cell complexes of mesoblastic origin, as described in previous slides, were also encountered (see table).

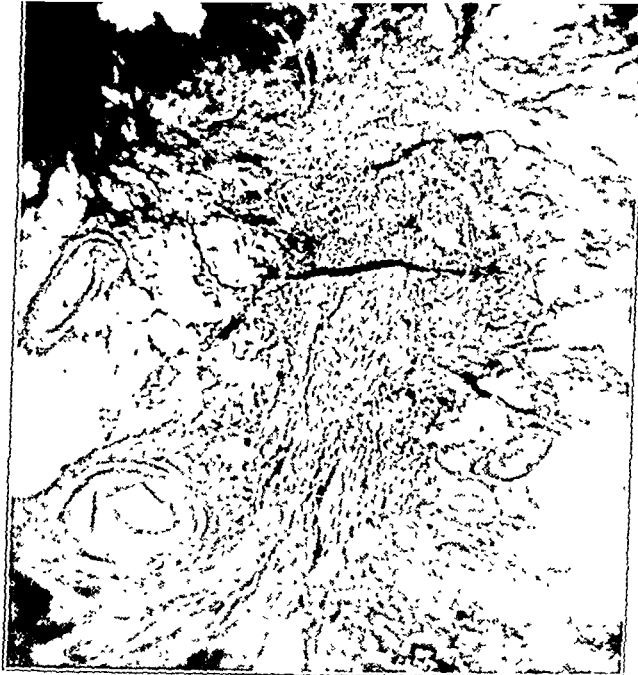


Fig. 10.—Ligated tail of the pancreas grafted into omentum. The tail was separated one year before; it had been grafted in the omentum for three months. There is evidence of a good blood supply; a firm sclerotic mass was embedded in omental fat.

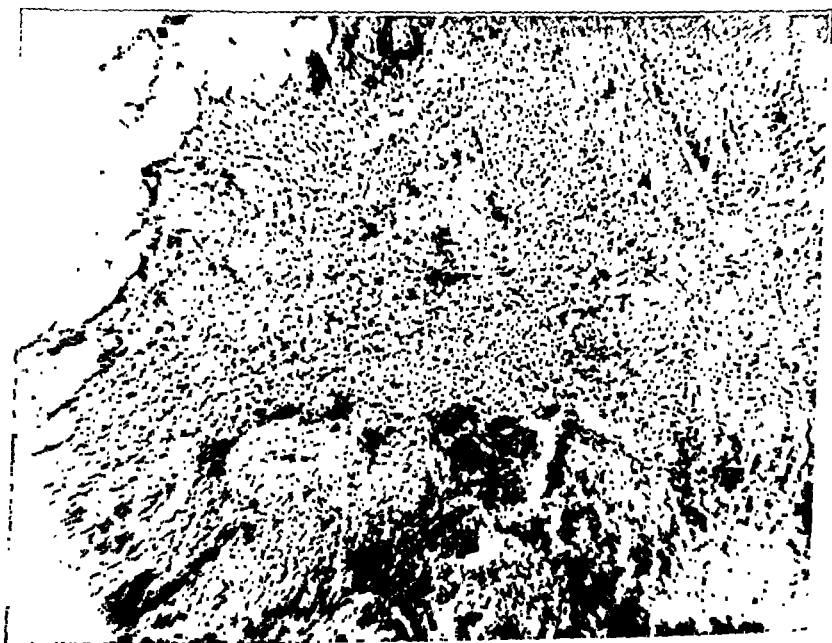


Fig. 11.—Same section as in figure 10, under high magnification. There are solid cell complexes surrounded by connective tissue, which may be identified with special stains as islands. Other groups of cells are seen, which consist of histiocytes and plasma cells, indicating the reaction of the omentum to the graft. No acini or ducts are seen.

OTHER OBSERVATIONS RELATING TO THE OPERATIVE PROCEDURE

The separation of the tail was first accomplished by throwing a wide tape around the body of the pancreas; also heavy linen ligatures and strips from the anterior rectus sheaths were used. When the abdomen was reopened at frequent intervals for obtaining histologic specimens, it was found that these ligatures would cause a marked inflammatory reaction with the outpouring of an exudate which in later laparotomies had organized into dense adhesions. In operations, when a ligature had been thrown around both head and tail for other purposes,⁹ the right lobe of the liver was invariably sealed down to the duodenum and could be separated only with some difficulty. There was no evidence of fat necrosis, for which careful search was made. Fat necrosis, however, was encountered when extensive charring of the pancreas was produced with the electric cautery.

It was also found that in spite of the marked fibrosis and foreign body reaction that occurred around such ligatures a reestablishment of continuity between the body and tail was not impossible, as in two dogs the acinar structures were well preserved and the ducts undilated three months after the operation.¹⁰ After this experience, the pancreas was doubly ligated and cut between two ligatures. The edema and exudation were just as marked as before, but I never encountered necrosis of the pancreas. As a matter of fact, it has been shown¹¹ that the pancreas may be simply severed and after ligation of the bleeding points be permitted to drain into the abdominal cavity without the appearance of necrosis in the pancreas.

The next modification was the use of Dr. Bovie's electric cautery. There was no need of ligatures either of the body or of the tail, and bleeders did not have to be tied. There was, however, a thin layer of desiccated tissue on either side of the cautery incision. At relaparotomy six weeks later, I found that the body and tail had been drawn together, and the original cautery incision could not be recognized without difficulty. This led me to interpose omentum between the two separated surfaces. This piece of omentum, which was wrapped around the separated tail, was examined histologically in six instances with regard to fat necrosis. In no case was it found.

The separation of the tail with the cautery, followed by wrapping it with omentum, was the technic finally adopted. In order to find out if the well vascularized omentum around the tail would hasten the absorption of cellular elements, free transplants of such tails that had been separated six months previously were made into the omentum and left

9. De Takats, G., and Nathanson, I. T.: The Effect of Ligation of the Tail of the Pancreas on Blood Diastase, *Arch. Surg.*, this issue, p. 788.

10 The reestablishment of continuity is not undesirable, as it seems to lessen the degree of sclerosis. This question will be discussed in a later communication.

11. Crandall, L. A.: Personal communication to the author.

for three months. A section of such a transplant showed enormous islands with mitoses, all signs of sufficient circulation without any evidence that these structures were being absorbed. Ukai³ saw islet tissue transplanted into the spleen after 450 days.

COMMENT

From the histologic studies it would appear that the separation of the tail of the pancreas from the rest of the gland results in a gradual disappearance of the acinar structures, replaced by fibrosis. There is no sudden necrosis "en masse" as would occur if the circulation was obstructed. It is possible, however, that circumscribed necrotic areas may result from acute or chronic pancreatic retention, as emphasized by Balo and Ballon.¹² The obstruction to the excretion of pancreatic juice must result in a greater intraductal pressure than the secretory pressure can overcome. The studies of Bensley¹³ have particularly emphasized that duct epithelium soon starts to proliferate, becomes columnar and shows infolding. I have found this in my slides. The islands do not show any change at first aside from an initial edema, but from the sixth week on there is evidence of proliferation in the islet cells, and more new islands are seen. Whether these islands originate in the persisting islands, from scattered islet cells in acini, from acinar cells or from the proliferating duct cells, is not my purpose to study. All I can state is that I am confronted with large cell complexes, which show the vascular arrangements and staining properties of islet tissue. Such cell groups do not seem to degenerate, even if transplanted into omentum. The intensity of sclerosis is probably variable in different species; it is much less marked in the guinea-pig or in the rabbit.¹⁴ A histologic study cannot give any information as to whether these cell complexes are functionally identical with islet tissue or whether their nervous control and physiologic response to stimuli are the same. Further work is necessary to study this question.

SUMMARY

1. The splenic portion of the pancreas was isolated from the rest of the gland in twenty-five dogs. The division with an electric cautery followed by wrapping omentum around the tail seemed the most satisfactory procedure.

2. Specimens were taken from the isolated tail at intervals of from two days to one year. After a short period of edema, a gradual destruction of the acinar elements takes place. There is an increasing amount

12. Balo, J., and Ballon, H. C.: Effects of Retention of Pancreatic Secretion, *Surg. Gynec. Obst.* **48**:1 (Jan.) 1929.

13. Bensley, R. R.: Studies on the Pancreas of the Guinea Pig, *Am. J. Anat.* **12**:297, 1911.

14. Bensley, R. R.: Personal communication to the author.

of connective tissue, first around and then within the lobules, and this finally results in pancreatic cirrhosis. The ducts are first dilated, then show proliferation and infolding of their epithelium; occasionally buds of epithelium form, resembling an early stage of embryonic development. A number of minute ducts also appear. The islands show edema for the first two weeks. Later there appear large solid cell complexes showing the vascular arrangement and staining properties of islet tissue. Fibroblasts may invade and break up the islets as the cirrhosis progresses.

3. Such an isolated tail does not tend to degenerate and undergo absorption for at least three months, if a free transplant of it is made into the omentum.

CORRELATIONS OF INTERNAL AND EXTERNAL PANCREATIC SECRETION

III. THE EFFECT OF LIGATION OF THE TAIL OF THE PANCREAS ON DIASTASE IN THE BLOOD *

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AND

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In previous communications,¹ I have described the histologic effects produced by separating the tail of the pancreas from the rest of the body. It has been known since the work of Wohlgemuth,² confirmed by Noguchi³ and by Gould and Carlson,⁴ that the diastase in the blood rises for a short time following ligation of the duct. Our histologic studies have shown the presence of marked edema of the separated tail for the first two weeks, later followed by a gradual atrophy of the glands of external secretion. In this series of experiments we have attempted to correlate our morphologic observations with values for diastase in the blood.

The purpose of this study was to establish with a simple test whether ligation of the tail would cause an increased absorption of pancreatic diastase. It was undertaken to establish the duration of the pancreatitis following ligation of the tail. As clinical experience has repeatedly shown, acute pancreatitis will cause a marked rise in diastase in the blood. In ninety-seven cases of acute necrosis of the pancreas collected by Schmieden and Sebening,⁵ seventy-eight cases (80 per cent) showed abnormally high figures. At the fifty-first German Surgical Congress,⁶

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† Elizabeth Ward Fellow in Surgery.

1. De Takats, G.: Correlations of Internal and External Pancreatic Secretion: I. General Considerations and Review of the Literature, *Arch. Surg.*, this issue, p. 771; Correlations of External and Internal Secretion: II. The Histologic Changes in the Isolated Tail of the Pancreas, *ibid.*, p. 775.

2. Wohlgemuth, J.: Das Verhalten der Diastase im Blut, *Biochem. Ztschr.* **21**:381, 1909.

3. Noguchi, Y.: Ueber die Fermentdiagnose bei Pancreasverletzung, *Arch. f. klin. Chir.* **98**:545 (May 21) 1912.

4. Gould, C. K., and Carlson, A. J.: Further Studies on the Relation of the Pancreas to the Serum and Lymph Diastase, *Am. J. Physiol.* **29**:165, 1911.

5. Schmieden, V., and Sebening, W.: Chirurgie des Pancreas, *Arch. f. klin. Chir.* **148**:319 (Oct. 27) 1927.

6. Discussion on paper of Schmieden, V., and Sebening, W.: *Arch. f. klin. Chir.* **148**:67 (Oct. 27) 1927.

Guleke, Unger and Heuss and von Redwitz emphasized the value of determinations for diastase in the blood or the urine. While it is recognized that determinations for lipase in the blood are a more sensitive index of pancreatic absorption,⁷ the simplicity and ease with which diastase can be determined in the blood made this test preferable. It can be carried out in about forty minutes and is therefore useful in emergencies.

METHODS OF EXPERIMENTATION

Normal healthy dogs were used in the first control series. After the injection of morphine, $\frac{1}{2}$ grain (0.02 Gm.), and atropine, $\frac{1}{60}$ grain (0.001 Gm.), ether anesthesia was induced. The abdomen was opened with a short midline incision starting just below the xyphoid process. The duodenum was pulled forward two or three times. In other words, all the factors that are present outside of pancreatic ligation and that might have influenced our values were introduced. The duodenum was then replaced in the abdominal cavity. In a series of five dogs the values for diastase were taken every second day before, and a week after, the operation.

Determinations for diastase were made according to the original method of Wohlgemuth, as described by Unger and Heuss.⁸ For the test the following materials were necessary:

2 cc. of blood serum (or urine)	2 pipets
1 per cent solution of sodium chloride	10 test tubes
1 per cent soluble starch	
Fiftieth-normal iodine solution	

About 10 cc. of blood is taken from the vein in a centrifuge tube, allowed to clot and separation of the serum permitted. One cubic centimeter of serum is pipetted into the first and second tubes. One cubic centimeter of 1 per cent solution of sodium chloride is pipetted into every tube. After the proper mixing of the serum and sodium chloride in tube 2, 1 cc. is again pipetted into tube 3. Here again after the proper mixing 1 cc. is pipetted over to tube 4, and so on up to the tenth tube, when the last cubic centimeter pipetted out of the tenth tube is discarded. To every tube 2 cc. of the soluble starch solution is then added, well mixed, and the whole system of tubes incubated in a thermostat at 38 C. for thirty minutes. At the end of that time, the fermentation is abruptly stopped by immersion of the tubes in cold water for a few minutes. Three drops of fiftieth-normal iodine solution are added to each tube. The undigested amylo-dextrin gives a blue reaction, the erythro-dextrin, red and the achro-dextrin, yellow. The end-point is read at the tube which shows the first trace of purple without being a solid blue. The quantity of ferment is calculated by raising the amount of starch (2 cc.) to the power which is indicated by the number of that test tube which is the last not to turn blue. For instance, if the end-point is at the fourth tube, $D = 2^4 = 16 \frac{38^\circ}{30}$, indicating at the same time the temperature and duration of incubation. The Wohlgemuth unit, then, is the amount of diastase which will digest 1 cc. of 0.1 per cent of starch solution in thirty minutes at a temperature of

7. Grassberger, A.: Diastase und Lipase Werte im Blut bei operativ gesetzten Pankreasverletzungen, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **41**:1, 1928.

8. Unger, E., and Heuss, H.: Zur Frühdiagnose der akuten Pankreasnekrose, Zentralbl. f. Chir. **53**:1500, 1926.

38 C. The diastatic values in the blood of the dog, $D = \frac{38}{24h}$, vary between 160 and 320.² Our normal figures taken in more than fifty individual determinations vary between 32 and 64, with an occasional reading of 96 following an incubation period of thirty minutes.

Following the exploratory laparotomy, determinations for diastase were made on the second, fourth, sixth, eighth and tenth days. We found that food, at least the food which the dogs are fed in the laboratory, does not influence values for diastase. Blood did not have to be taken then on the fasting animal.

In a second series of experiments, the tail of the pancreas was ligated as described in a previous communication,⁹ and determinations for diastase were made every second day for two weeks.

In a third series of experiments, not only the tail but the head of the pancreas was ligated with a double silk ligature. Thus, only about the size of a quarter

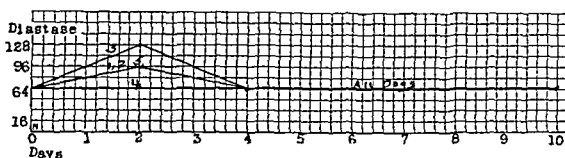


Chart 1.—Diastatic values in the blood following an exploratory laparotomy with the animal under ether anesthesia, with the preliminary medication of morphine and atropine. The duodenum was pulled forward and the pancreas lightly grasped. The maximum rise is 128, average rise, 96. Numbers 1, 2, 3, 4 and 5 indicate the five dogs used in this control series.

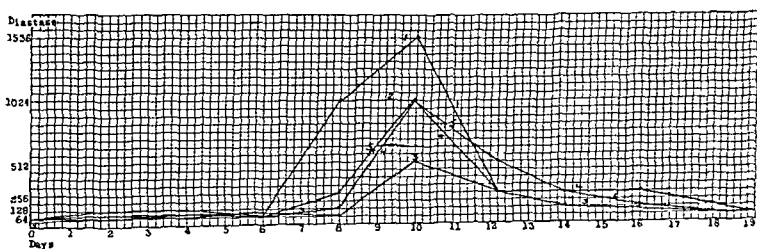


Chart 2.—Diastatic values in the blood following ligation of the tail of the pancreas. There is a small initial rise, comparable to that of the first chart in dogs used as controls, but more protracted, and a sharp secondary rise between the sixth and eighth days. The peak in this series is reached on the tenth day, after which there is a sharp drop.

remained around the main duct for the purposes of external secretion, while the rest of the gland was barred from secreting into the duodenum. Thus, a maximum amount of ferment absorption could be expected without the elimination entirely of the secretion into the duodenum.

RESULTS

Following an exploratory laparotomy with the animals under ether anesthesia, with preliminary medication of morphine and atropine, there

9. De Takats (footnote 1, second reference).

was no appreciable rise in diastase in the blood. The maximum rise on the second day was $D \frac{38}{30} = 128$, the average rise, 96 (chart 1). The ligation or isolation of the tail of the pancreas resulted in a small but definite initial rise, followed by a second marked rise beginning between the sixth and eighth days. The diastase in the blood rose to 1,024 and 1,536 (chart 2). In a third series, in which both the head and the tail were ligated, sharp immediate rises were observed up to 3,072. About the tenth day, the values came down to normal and remained so (chart 3).

Chart 4 shows the average values of the three series of experiments on a total of fifteen dogs.

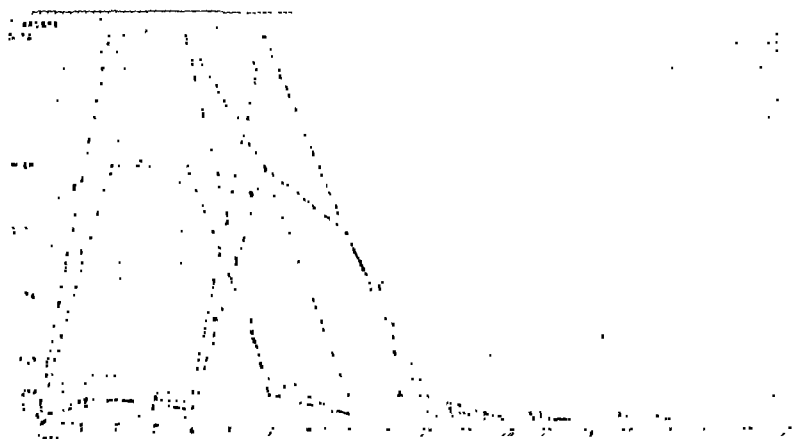


Chart 3.—Diastatic values in the blood following ligation of both head and tail of the pancreas. There is a sharp early rise, and a sudden drop on the tenth to twelfth days, after which the diastase does not rise.

COMMENT

Values for diastase in the blood of the normal dog seemed fairly constant and varied from 32 to 64 with the technic described. Food or an exploratory laparotomy did not influence these values to any extent. The ligation of the tail of the pancreas resulted in a small initial rise followed by a large secondary rise in the diastase in the blood. Such a secondary rise was described after ligation of the pancreatic duct by Gould and Carlson. They expressed the belief that the second rise occurred when the zymogenic cells recuperated from the edema which followed the operation. In our histologic studies, edema was the dominating picture observed immediately following ligation. As it subsides around the tenth day following operation, the coincidence of such histologic observations with the rise in diastase in the blood is striking. The amount of gland tied off at the operation seems to influence the diastatic values. In the third series, in which both the head and the tail

were ligated, the diastase rose to enormous values soon after operation. No secondary rise was noted, however, as if by that time there was no further excretion of diastase. At all events, this determination seems to be a sensitive index of acute pancreatic obstruction. That it gives only increased values in acute conditions has often been emphasized clinically. This is easily understood if we consider that the acini, the excreting ducts of which are obstructed, undergo degeneration as reported in our histologic study. The fact that the high diastasic values following glandular ligation return to normal within two weeks might be interpreted in a way that acinar elements in the ligated portion have ceased to excrete. This question is now under investigation with another method of approach. The formation of a pancreatic fistula from the

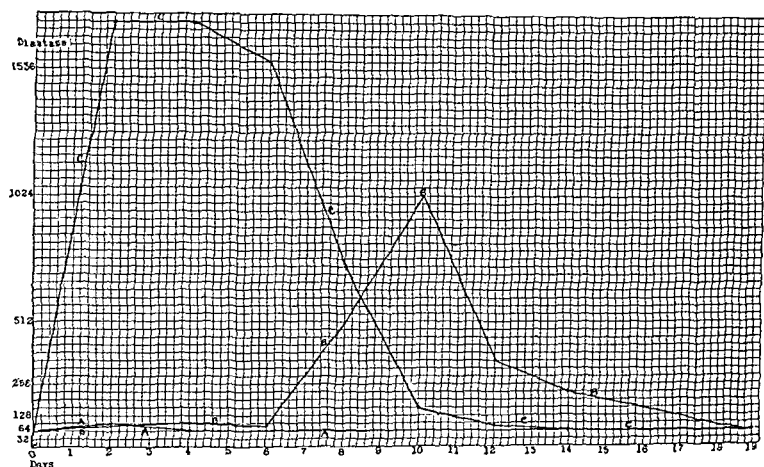


Chart 4.—Average curves of charts 1, 2 and 3. The small early rise following ligation of the tail is more protracted than in the control animals. The secondary rise in dogs with ligation of the tail shows its peak when the enormous rise following ligation of the head and tail has almost subsided (tenth day). *A* shows the average curve for the dogs used as controls; *B*, that for dogs on which ligation of the tail was done, and *C*, that for dogs on which ligation of both the head and the tail was done.

isolated tail is not probable, if the obstruction can be maintained for two weeks.

The original test of Wohlgemuth is simple and rapid and can be carried out without any special apparatus. We were especially interested in using such a test because of the possibility of a wider clinical use. We are aware that this method has been modified repeatedly and other methods described. Some insist on the use of buffer solutions in order to establish an optimal p_H for diastasic activity. A recent article of Elman and McCaughan¹⁰ measured the lowering of the viscosity as

10. Elman, R., and McCaughan, J. M.: The Quantitative Determination of Blood Amylase with the Viscosimeter, *Arch. Int. Med.* 40:58 (July) 1927.

effected by the starch-splitting ferment. While the importance of the buffers is clear in determinations of diastase in feces and urine, the buffer system of the blood is a reasonable safeguard that large variations in p_H will not occur. While the optimal p_H may not be thus obtained, the figures are comparable. The use of buffer solutions complicates the method without being of marked advantage. A few comparative determinations with the buffer method of Stafford and Addis¹¹ convinced us that buffering in the blood is not of any advantage. Our curves showing the amount of diastase following ligation of the tail or the head and tail show that a definite and constant rise is estimable.

We have no experience with the interesting method of Elman and McCaughan, as our work was completed at the publication of their method. These authors made the statement that diastase in plasma deteriorates rapidly, whereas diastase in serum retains its potency. We have used diastase in serum all through our work and have kept serums in the icebox for two days without deterioration. Checks on the p_H of serum have shown no change in the serums which would warrant buffering.

Another advantage of determining diastase in the blood instead of in the urine is the factor of concentration and the rate of excretion of urine, as has been emphasized by Stafford and Addis. Determinations of diastase with feces introduce additional difficulties, as recently discussed by Wolfer and Christian.¹² The clinical application of a simple determination of diastase in the blood in suspected pancreatic injuries and in acute necrosis of the pancreas is well worth considering. No increase can be expected in chronic pancreatitis and obstruction.

SUMMARY

1. Isolation or ligation of the tail of the pancreas leads to an early increase in diastase in the blood, followed by a secondary rise about the seventh day. From our previous histologic studies, we believe that the secondary rise may be due to the disappearance of the initial edema.
2. The rise in diastase seems to be proportionate to the amount of tissue ligated. The ligation of both the head and the tail of the pancreas gave much higher rises in diastase than ligation of the tail alone.
3. The return of the diastasic values to normal at the end of two weeks would indicate that external secretion is not to be expected or feared from the ligated portion after two weeks.

11. Stafford, D. D., and Addis, T.: Diastase Determinations in Urine and Blood as a Method for the Measurement of the Functional Capacity of the Kidney, *Quart. J. Med.* **17**:151, 1924.

12. Wolfer, J. A., and Christian, L. W.: Pancreatic Function Tests, *Arch. Surg.* **17**:899 (Dec.) 1928.

EXPERIMENTAL SARCOMA OF BONE*

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It is known that an experimental tumor on transplantation invariably reproduces the same kind of tumor as to cell type. For instance, the Rous sarcoma always produces a fibrosarcoma whether it is injected into muscle, bone, connective tissue or an internal organ, such as the liver. When, therefore, an opportunity came to work with an endothelioma, I seized the chance to observe its behavior when injected into the bone-marrow of chickens. The purpose of such a procedure was several fold. First, it was desired to see to what extent it might produce a tumor resembling the much disputed tumor described by Ewing as an endothelioma of bone. Second, it seemed important to watch the development of tumor of the bone-marrow from its inception, a thing impossible to do in man, since in the latter it usually has advanced considerably before it is discovered. Third, the reaction of the bone itself to the presence of cells of known origin might throw some light on the type of cell that is capable of forming bone.

This tumor was found by J. A. Murray, director of the Imperial Cancer Research Fund, London, in a Rhode Island Red chicken. It was furnished me through the courtesy of Dr. W. E. Gye. The material received had been dried in London three weeks before it was used. It was said by Murray that filtrates of the tumor, as well as suspensions of the cells, would reproduce the tumor on injection into an homologous strain of chickens. The new tumors therefore presumably arise from cells of the new hosts, and not from the transplants.

Murray, in a communication through Dr. Gye, said that by serial sections he had observed the tumor arising from the lining cells of blood vessels. My first experiment was an attempt to prove this. Suspensions of the tumor cells were injected into the thigh muscles of chicks, and the animals were killed at various intervals in order to watch the development of the resulting tumors. Into half the chicks, a small amount of ground carbon was injected with the tumor cells in order that the sites of the inoculated material might be localized. The tumors grew, as a rule, rapidly. Within thirty-six hours, microscopic nodules were present between the muscles. When carbon also was present, growth was even

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* Part of this work was done in the Department of Pathology, Harvard Medical School. The x-ray pictures were made at the Peter Bent Brigham Hospital, Boston, under the direction of Dr. M. S. Sosman.

more rapid. Carbon alone, injected into several control chicks, or into the opposite thighs of the chicks receiving tumor cells, caused a proliferation of the same kind of cells as those which formed the tumor. This proliferation never became malignant, but remained as a typical foreign body reaction. Both the tumor cells and the cells responding to the injection of carbon alone were phagocytic. Many of them became filled with the carbon (fig. 3).

Because of the rapidity of growth and the intimate intermingling of tumor cells, blood vessels and connective tissue, it was not possible to say,



Fig. 1.—An early stage of the tumor, starting in the muscles of the thigh. The cells appear to be growing from the sarcolemma, and are forming sinuses; $\times 80$.

beyond the shadow of a doubt, from which cells the tumors arose. In muscle, the first cells to appear seemed to come from resting cells between the muscle or the connective tissue fibers, or perhaps from the mesothelium forming the surface cells of the sarcolemma. These cells were undifferentiated and contained considerable lightly staining cytoplasm and round or oval nuclei with prominent nucleoli. They resembled the reticular cells of man more closely than the endothelial type of cells. The former have a reticulated chromatin, the threads of which commonly join at a concentrically placed nucleolus; in the latter, the chromatin is

in finely scattered granules, among which nucleoli can often not be distinguished. The cells of the tumor in the chicken thus resembled the cells lining lymph sinuses, and were comparable to the Dorothy Reed cells of the Hodgkin's type of lymphosarcoma. They formed spaces and lined them (fig. 1), and some of the spaces contained blood. Mostly, however, the tumor grew in lobulated masses, and had a capillary stroma, except where thin bands of fibrous tissue divided up the tissue.

In bone-marrow, the tumor cells appeared to arise from the indifferent cells lining the marrow sinuses, and appeared first as spindle cells without fibrillae. Here, again, it was impossible to say from which type



Fig. 2.—A proliferation of cells in the bone-marrow four days after the injection. Carbon is present. There was no evidence of tumor in the x-ray picture; $\times 80$.

of cells the tumor cells arose. There seemed to be a general reticular hyperplasia, and the cell which became a tumor cell could not be distinguished from a similar (or identical) cell which formed the blood cells. Carbon pigment stimulated the proliferation of the same kind of cell here also.

In transplantations of the tumor cells into the bone-marrow, young chicks from 3 to 10 weeks old were used. It was comparatively easy to inject the ground-up tumor suspended in salt solution into the marrow cavity of the tibia through the proximal articular surface. The animals were killed from time to time, some as early as twenty-four hours after the inoculation. X-ray pictures were made from the first day, until it

was found that tumors could not be demonstrated before about the fourteenth day. Sixty-five chickens were used, and practically all developed tumors. The results, in those which were allowed to run the full course, were about the same. Therefore, to be brief, only a few cases will be given in detail.

At twenty-four hours, no tumor could be observed microscopically. Tumor cells which had been injected could be identified in some cases, and these were undergoing autolysis. On the second and third days following the injection, a reaction on the part of the marrow could be observed as a proliferation of undifferentiated cells. These cells appeared

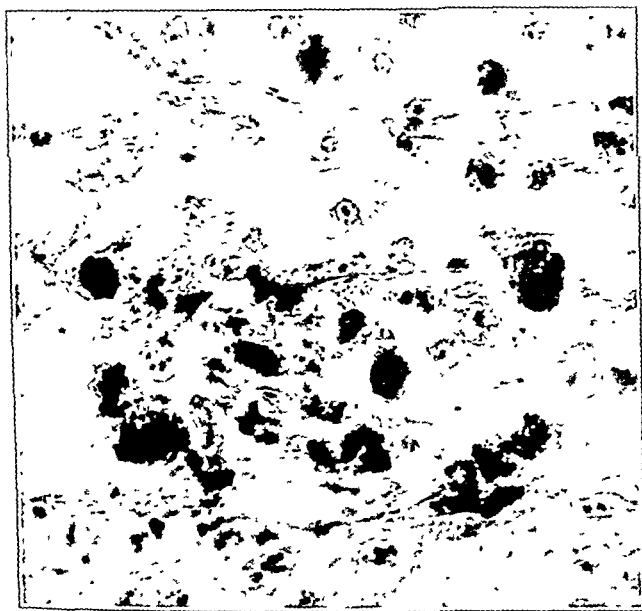


Fig. 3.—A higher magnification of the cells four days after the inoculation with the tumor. Their phagocytic character is shown; $\times 480$.

no different from those which presumably were forming white blood cells, and at this time a definite diagnosis of tumor could not be made. In those cases in which carbon had been injected, the cells were phagocytosing the pigment. Definite tumor could be diagnosed on the fourth day in four chicks by microscopic examination (fig. 4). The cells at this stage were of spindle shape, but staining with phosphotungstic acid hematoxylin failed to demonstrate fibrogia.

At later stages, the tumor grew up and down the medullary cavity, though in most cases the tumor reached the outside before entirely replacing the bone-marrow. Tumor could not be demonstrated by palpation or by the x-rays in any chick before the fourteenth day. Of ten

chicks that were allowed to live beyond this period, one contained a palpable tumor on the fourteenth day, three on the fifteenth, two on the sixteenth and two on the eighteenth. The x-rays revealed tumors in one chick on the fourteenth day, in two on the fifteenth and in one on the sixteenth. These were animals which had been followed systematically by taking daily pictures. Two such chicks died before palpable tumors appeared, one on the fifteenth day and one on the nineteenth day. Each of these contained metastases in the liver and the spleen, and gross tumor was present in the tibia (on longitudinal sectioning),

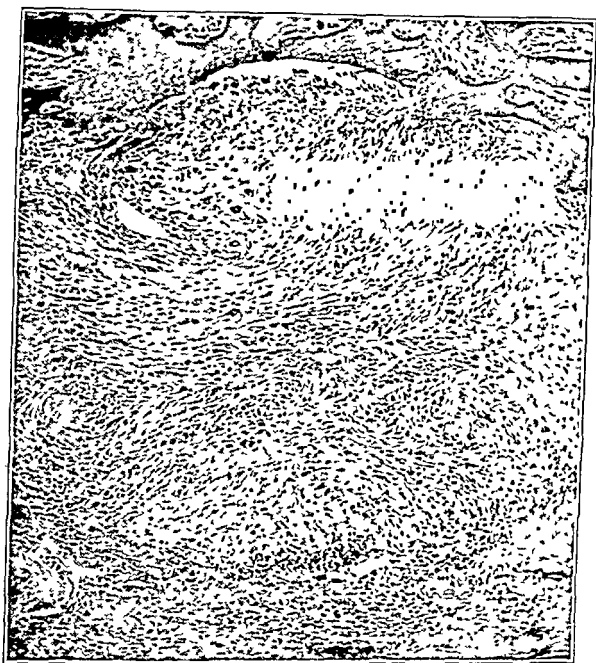


Fig. 4.—The picture shows the size of the tumor of the bone-marrow at four days. No carbon was injected. No tumor was shown by the x-rays; $\times 80$.

but tumor could not be diagnosed from postmortem x-ray pictures. All the chicks that were allowed to die of tumor succumbed before the twenty-second day following the injection. The clinical course of one chicken is given as an example of the usual progress of the tumor.

Chicken 36.—A suspension of cells from a large tumor of the thigh was injected into the left tibia of chick 36 when it was about 2 months old. X-ray pictures were made daily, beginning on the sixth day, until the death of the chicken, on the eighteenth day. The tumor became visible on the sixteenth day (fig. 5 A); a slight roughening of the periosteum was shown, with a suggestion of fine, radiating lines. On the seventeenth day (fig. 5 B), both sides of the shaft showed rarefaction and had a mottled, ragged appearance, and radiating lines

and an elevated periosteum were present on one side. Fig. 5 *C* shows the tumor on the eighteenth day, when a definite fusiform thickening of about a third of the shaft could be detected.

At autopsy, huge metastases were found in the liver and metastases also in the lungs and the spleen. The tibia contained tumor throughout the marrow cavity, and this had broken through in the region of the nutrient artery to form a subperiosteal mass which completely encircled the cortex. Between the periosteum and the cortex there was a new formation of bone. In the medullary portion, the tumor was soft and gray and contained numerous small areas of necrosis (figs. 6 and 7 show a more advanced tumor of similar appearance). Histologically, the tumor consisted of the type cells, previously described, in a capillary stroma. These cells seemed to be differentiating into the cells that were forming bone beneath the periosteum.

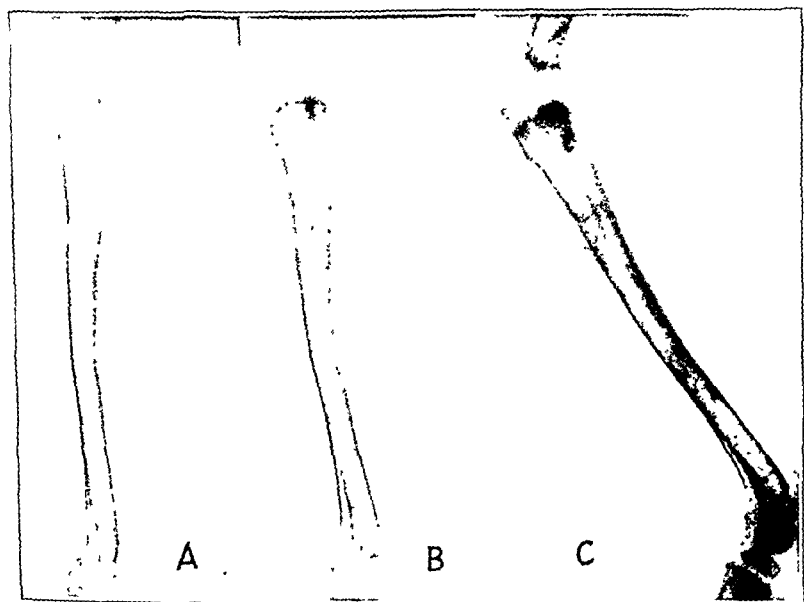


Fig. 5 (chick 36).—*A*, the first definite evidence of tumor shown by the x-rays, on the sixteenth day; *B*, the tumor on the seventeenth day, showing rapid growth; *C*, the tumor on the eighteenth day, on which the chicken died. The x-ray picture is of the detached leg.

A single experiment was undertaken with the Rous fibrosarcoma for purposes of comparison with the endothelial tumor. A cell suspension received from Dr. J. H. Mueller of the Department of Bacteriology, Harvard Medical School, was injected into two barred Plymouth Rock chickens. The site of injection was, as in the case of the endothelial tumor, the tibia. One animal was killed on the sixteenth day. A definite tumor was present, which was passing out into the subperiosteal space around the nutrient artery (fig. 8). The second chicken was killed on the twenty-first day. A fusiform tumor was found similar to

that formed by the endothelioma. The cells of the tumor were apparently forming the bone that was present in considerable amount between the periosteum and the cortex.

The endothelial tumor was not an exact reproduction of the endothelial myeloma of Ewing. It had characters both of Ewing's tumor



Fig. 6.—A tumor that caused death in twenty-one days with generalized metastases. The medulla is filled with tumor, the cortex is eroded and masses of tumor and new bone are present between the periosteum and the cortex; $\times 4$.

and of osteogenic sarcoma. The type cell, as has been said, was different, though the cells of chickens do, in general, differ from the cells of man in several respects. The tumor grossly resembled Ewing's tumor in that it fairly well filled the marrow cavity, it occupied more than a third, sometimes nearly all, of the shaft, and it had osteolytic rather

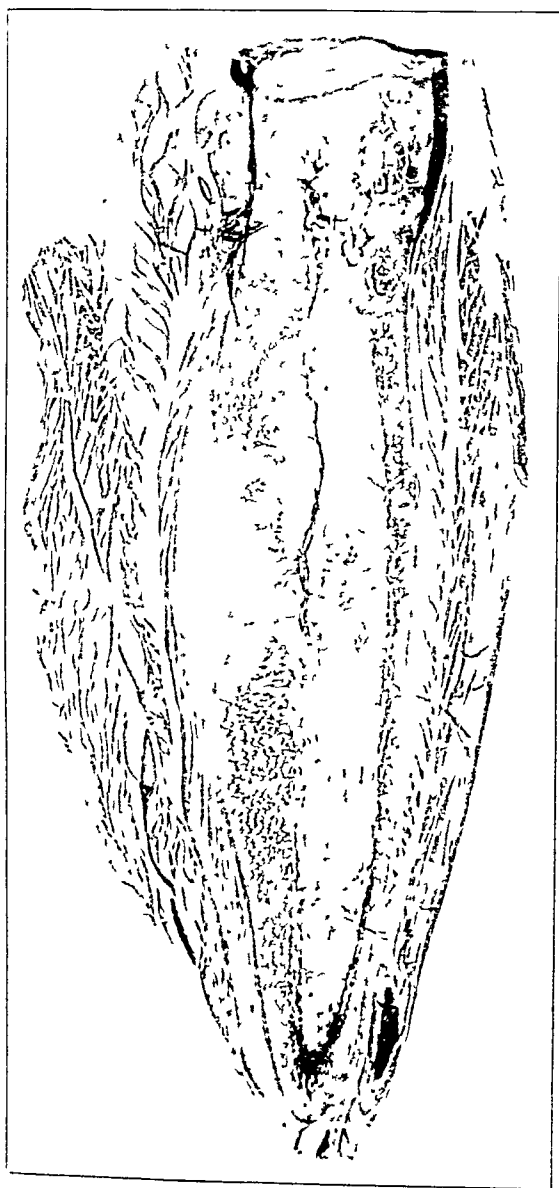


Fig 7.—The tumor forms bone only when confined beneath the periosteum. At one place in this section, where the periosteum has broken down, no bone is formed, $\times 4$ Figure 11 shows the x-ray picture of this bone

than sclerosing properties while confined to the medulla and the cortex. It was pointed out previously¹ that any tumor of bone (metastatic or primary) may cause the formation of radiating spicules as seen by the x-rays. This, however, is much more common in osteogenic sarcoma than in other tumors, and is one of the least conspicuous features in Ewing's tumor. The method of growth of this experimental tumor beneath the periosteum exactly duplicated a subperiosteal osteogenic sarcoma as seen in man. Such tumors were previously called periosteal sarcomas, until Codman² pointed out that all of them are both medullary and subperiosteal, and claimed that all arose in the medulla. The



Fig. 8.—Rous sarcoma. This shows one way by which the tumor passes out of the medullary cavity: the cells infiltrate along the nutrient artery and form a subperiosteal tumor; $\times 80$.

tumors in the chickens illustrated admirably two ways by which a medullary tumor reaches the subperiosteal region: one by way of the nutrient foramen, and another by growing between bone spicules and along the haversian systems (figs. 8 and 9).

So far as the second purpose is concerned, that is, the following of a tumor of bone from its inception to its termination, there may be

1. Connor, C. L.: Endothelial Myeloma, Ewing, Arch. Surg. **12**:789 (April) 1926.

2. Codman, E. A.: The Nomenclature Used by the Registry of Bone Sarcoma. Am. J. Roentgenol. **13**:105, 1925.

differences of opinion as to how far one may go in comparing a tumor in the chicken to one in man. Generally, in man, a tumor has been present for a considerable period before attention is called to it by some untoward occurrence, but usually there is no means of ascertaining how long. The factor of pain, of course, was not evident in the tumors in the chickens, if present. Most of the chicks showed no signs of distress until metastases were far advanced. Two only limped, and each of these had developed small nodules on the articular cartilage at the site of injection. Pain, as a rule, is the symptom that draws attention to a tumor of bone in man, although cases are not infrequent in which a spontaneous



Fig 9.—Another way in which a subperiosteal tumor is formed: the cells of an endothelioma infiltrate through bone trabeculae and pass along beneath the periosteum; $\times 80$.

fracture is the first sign. One cannot compare the two growths, therefore, in this respect. One may only record that, in the chickens, fully two thirds of the course of the tumors had been run before they were detectable, in spite of the fact that first signs were eagerly awaited.

There has been discussion regarding the nature and causes of the new formation of bone in both primary and metastatic tumors of bone. It is fairly well agreed that the formation of new bone around a metastatic carcinoma or a giant cell tumor is a reparative, reactive or defensive process, similar to the fibrosis occurring around tumors in soft tissues.

But it is conceded that osteogenic tumors form tumor bone, and many older pathologists professed to distinguish between bone formed by tumor cells and that formed by normal osteoblasts. Many osteogenic tumors form abortive or malformed bone, but many also form bone that is indistinguishable from that seen in a normal callus. Eising,³ on philosophical evidence, believed that the bone formed in all tumors is reactive, and not formed by tumor cells. It seems reasonable, however, that osteoblasts in an osteogenic tumor might form an osseous tissue just as fibroblasts in a fibrosarcoma may, and do, form collagen.



Fig. 10.—Formation of bone, apparently by tumor cells, between the periosteum and the cortex; $\times 80$.

Granting, then, that tumor cells may form bone, from what cell or cells may osteoblasts be derived? In most cases, these undoubtedly arise from spindle cells (fibroblasts?) of the periosteum and endosteum. The latter, however, is in man a rather indefinite membrane, and in young animals osteoblasts may apparently be derived from the marrow.⁴

3. Eising, E. H.: Bone Formation in Osteogenic Sarcoma: Teleologic Considerations, *Arch. Surg.* **12**:867 (April) 1926.

4. Keibel and Mall: *Human Embryology*, Philadelphia, J. B. Lippincott Company, 1910, vol. 1, p. 303.

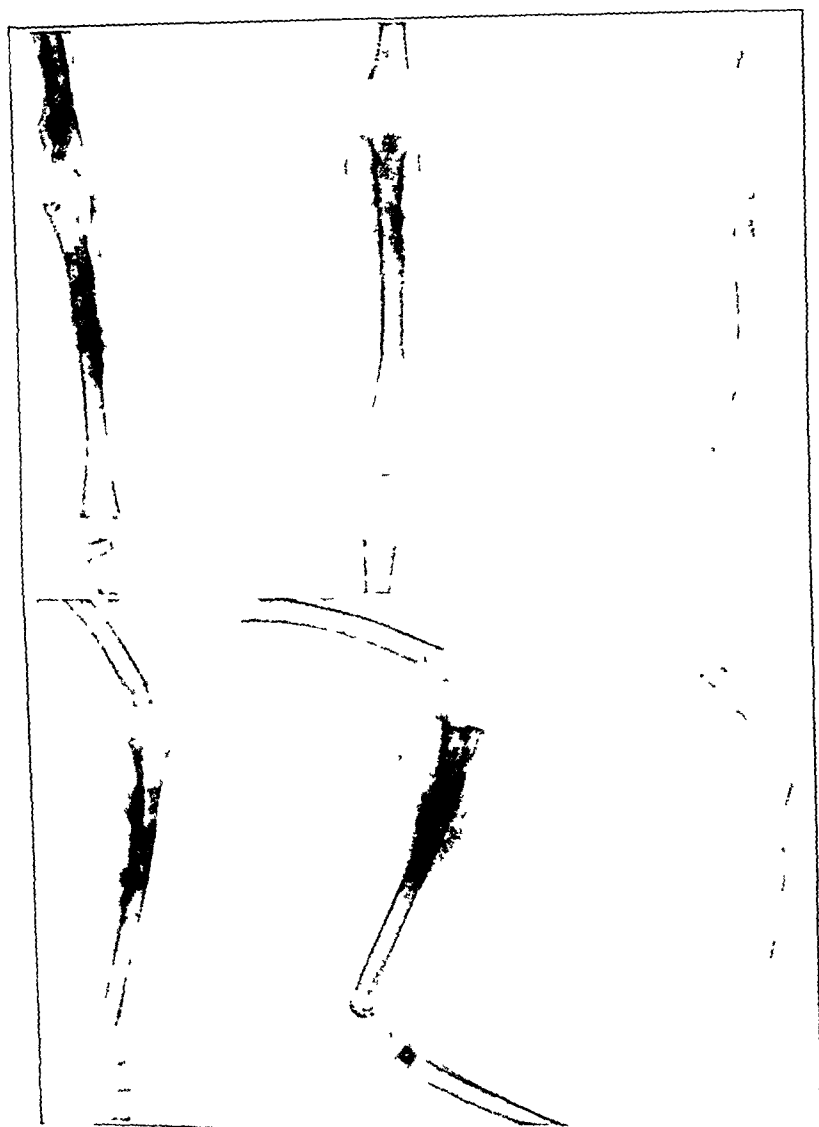


Fig 11—Three stages of growths in chicks of the same age, all at twenty-one days

Moschcowitz,⁵ discussing heterotopic formation of bone, declared that the osteoblast comes from an endothelial cell lining blood vessels, and further stated that a common cell (fibroblast?) forms the endothelial cell, the osteoblast and the bone-marrow cell. Maximow⁶ derived the histiocyte, the fibroblast and the reticular cell from a common mesenchymal cell, and the osteoblast from the fibroblast. Fibrils, similar to those of a fibroblast, may be formed by the monocyte in tissue cultures.⁷

In the present experiments, two types of tumors, a fibrosarcoma (Rous) and an endothelioma (or reticuloma), produced bone under one condition only, namely, when the cells were confined between the periosteum and the cortex. There are probably three reasons for this: (1) both types of cells are capable under certain conditions of forming osteoblasts; (2) the conditions are probably a suitable physicochemical milieu, such as is found in the region of bone, and (3) a mechanical restraint similar to that caused by tumor growing between a tautly drawn periosteum and the cortex of bone. Once the periosteum has been broken through, the tumors grow much more rapidly, and no intercellular substance of any kind is produced by the endothelioma.

SUMMARY

A spontaneous transmissible endothelioma of the chicken was introduced into the marrow cavity of the tibia of the chicken for the purpose of duplicating, if possible, a tumor similar to that described by Ewing as an endothelial myeloma, and in order to watch the development and manner of growth of such a tumor. The resultant tumor resembled, in some respects, both endothelioma and osteogenic sarcoma as seen in man. Like endothelioma, it occupied a large part of the shaft and was osteolytic until it had penetrated via the nutrient foramen or through the cortical spicules to the subperiosteal space. While confined between the periosteum and the cortex, the tumor cells formed radiating spicules of bone. In a similar experiment with the Rous fibrosarcoma, it, too, formed bone beneath the periosteum.

Fully two thirds of the course of the tumor had been run before the tumor became palpable or visible by the x-rays, although it was

5. Moschcowitz, E.: The Relation of Angiogenesis to Ossification, *Bull. Johns Hopkins Hosp.* **27**:71, 1916.

6. Maximow, A. A.: Relation of Blood Cells to Connective Tissue and Endothelium, *Physiol. Rev.* **4**:533, 1924.

7. Fischer, A.: Sur la transformation in vitro des gros leucocytes mononucléaires en fibroblasts, *Compt. rend. Soc. de biol.* **92**:109, 1925. Carrel, A., and Ebeling, A. H.: Pure Cultures of Large Mononuclear Leucocytes, *J. Exper. Med.* **36**:365, 1922. Maximow, A. A.: Development of Nongranular Leucocytes (Lymphocytes and Monocytes) into Polyblasts (Macrophages) and Fibroblasts in Vitro, *Proc. Soc. Exper. Biol. & Med.* **24**:570, 1927.

present in all the bones examined on the fourth day. By the twenty-second day, the chickens had died with widespread metastases. Two died of metastases before a tumor could be demonstrated by palpation or by the x-rays, although tumors were present in both cases.

It is shown that both endothelial (or reticular) cells and fibroblasts are capable of differentiating into osteoblasts under certain physical and chemical conditions.

PULMONARY ATELECTASIS AND RESPIRATORY FAILURE *

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NEW YORK

In an earlier publication, I ¹ described the abrupt onset of respiratory embarrassment in cases of caseous pneumonic phthisis complicated by sudden atelectasis. Observation of a large number of severe and extensive cases of acute phthisis has convinced me that this complication is not the exception, but rather the rule, in such severe processes of the lungs. To illustrate the extent to which such conditions may progress, a case is here presented which is only one of many such observations. This particular case was chosen because it shows atelectasis of an entire lung which cleared up ultimately, in spite of catastrophic progress of the process itself. Furthermore, since this patient died of a miliary dissemination shortly afterward, an opportunity was afforded to check up on the pathologic changes.

The patient, J. G., aged 25, a bank clerk, became ill suddenly about six weeks previous to his admission, in the first days of January, 1925. His first roentgen examination is not reproduced here, as it was not much different from the plate given here with the date of March 4, 1925. The patient was too ill for any active therapy to be attempted. On April 9, 1925, he developed symptoms of acute respiratory distress. The plate of that date (fig. 2) reveals as the reason for the attack a massive atelectasis of the entire left side of the lung. Figure 3, taken on May 15, 1925, shows reinflation of the formerly collapsed lung, except for some extension of the process into the lower lobe, as compared with the first plate. The patient died two months later. Autopsy revealed vast honeycombing throughout the left lung, with cavities of different sizes and shapes. The intervening pulmonary tissue was studded with tubercles. The pleura of the left side was densely adherent. The right lung showed lobular involvement in the upper lobe and miliary dissemination throughout the rest of the lung.

Here, then, was a case in which spread of an acute exudative process from the upper to the lower lobe was accompanied by a temporary collapse of the entire lung. Atelectasis and retraction of severely affected lungs in the course of phthisis has been described in the literature repeatedly; recently Packard ² reported such cases. More or less atelectatic collapse of severe tuberculous lesions has been observed to be a regular feature of phthisis. That atelectasis is also a regular

* Submitted for publication, April 29, 1929.

1. Rappaport, I.: *Am. Rev. Tuberc.* 18:447, 1928.

2. Packard, E. H.: *Am. Rev. Tuberc.* 18:7, 1928.

feature of other severe pulmonary diseases has become increasingly evident within the last decade. Churchill and Holmes³ reported atelectasis in pulmonary suppuration of pyogenic etiology. The Philadelphia workers on atelectasis conclusively demonstrated its presence in all post-operative complications of the lungs. Coryllos and Birnbaum⁴ recently presented experimental evidences to prove that atelectasis is the underlying pathologic change of all pneumonic processes.

In short, there is ample clinical and pathologic evidence to the fact that pulmonary processes of whatever etiology are accompanied by atelectasis of greater or lesser areas of the lungs. The clinical symptoms

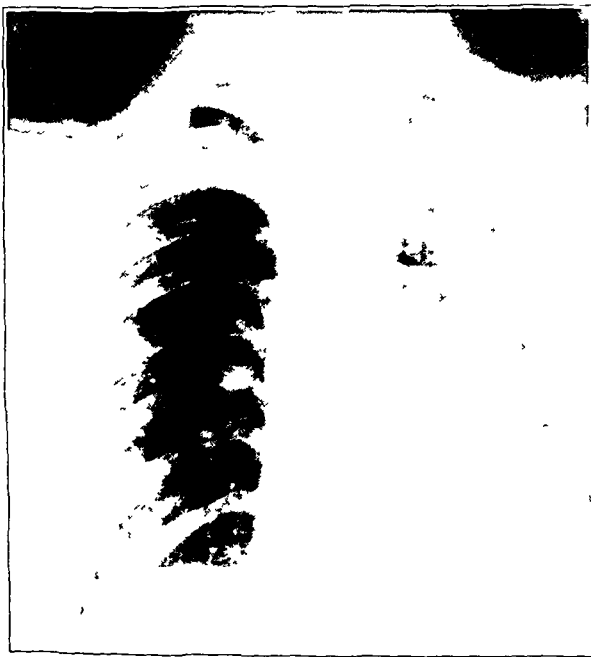


Fig. 1.—Lungs of the patient, J. G., taken on March 4, 1925

of atelectasis are identical, regardless of the underlying pulmonary disease. The symptoms of critical pneumonia, massive collapse or any other critical condition of the lungs are exactly the same; they are those I have described under the name of "anoxemic cardiac syndrome." They are the symptoms of acute respiratory embarrassment, which vary in intensity according to the proportion of breathing surface failing

3. Churchill, E. D., and Holmes, G. W.: Lobar Atelectasis in Chronic Pulmonary Suppuration, *Arch. Surg.* **14**:1093 (May) 1927.

4. Coryllos, P. S., and Birnbaum, G. L.: Lobar Pneumonia Considered as Pneumococcic Lobar Atelectasis of the Lung: Bronchoscopic Investigation, *Arch. Surg.* **18**:190 (Jan.) 1929.

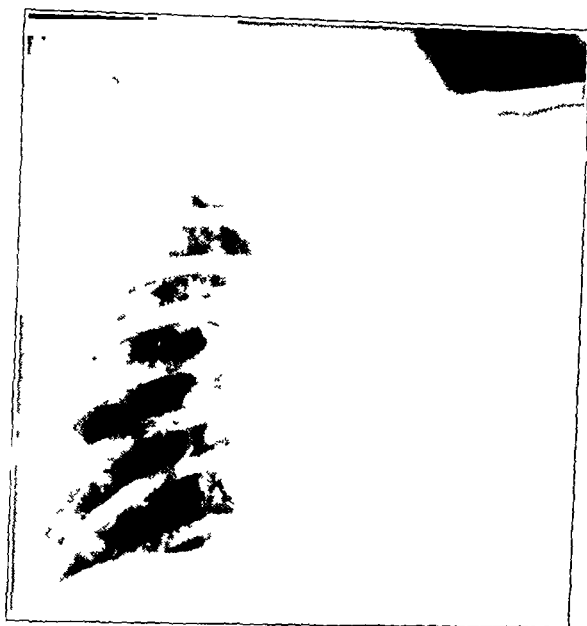


Fig 2—Lungs of the patient, J G, taken on April 9, 1925, showing a massive atelectasis of the entire left side of the lung



Fig 3—Lungs of the patient, J G, taken on May 15, 1925, showing re-inflation of the formerly collapsed lung except for some extension of the process into the lower lobe

in function, and according to the compensatory capacity of the breathing surface remaining in function. In the aforementioned paper on the respiratory failure syndrome, I have described its acute form and emphasized that it shows a wide range of variations according to the degree of respiratory dysfunction present. As a basis for the discussion in that paper, I adopted the present day pathologic concept that respiratory embarrassment leads to failure by way of cardiac exhaustion and that the clinical phenomena are therefore cardiac in origin. However, even at the time that the paper was published I believed in a different conception of respiratory failure, but I was not yet ready to bring out the subject in the light of my own conceptions.

The recent studies, experimental as well as clinical, with the revival of the discussion of pulmonary atelectasis in the literature, afford me the opportunity to attempt the presentation of my own conceptions. My studies of respiratory failure date back to the last twelve years of clinical observation of a great number of respiratory failures in such wartime mass affections of the lungs as epidemics of influenza, pneumonia and gassing. These clinical observations have convinced me that respiratory failure is never associated with cardiac failure, and that chronic respiratory failure leads only to a relative circulatory insufficiency, but not to cardiac failure. My clinical observations have brought me to the conclusion that pulmonary atelectasis is the pathologic substrate of the clinical entity of respiratory failure. Pulmonary atelectasis and respiratory failure are the two sides of the selfsame clinicopathologic process. Respiratory failure, of whatever etiology—suffocation, infection or obstruction—always appears with atelectasis as the pathologic, and the “respiratory failure syndrome” as the clinical, accompaniment of the disease.

An attempt will be made to present this conception and the physiologic, pathologic, experimental and clinical data supporting it.

In these days of functional medicine it is not customary to propose changes of theoretical conceptions without offering some new and personally produced experimental evidences. I have no such evidence, as mine is purely clinical. Disease is nature's great biologic experiment that unrolls itself before the eyes of the clinician. The respiratory conditions here discussed are of a purely functional nature and run their course like true experiments. The old problem of pulmonary collapse has now been revived, owing to the fact that x-rays have demonstrated it to be the center of events in almost every form of pathologic process of the lungs. Besides the problem of collapse of the lungs, respiratory pathology is riddled with unsolved problems, such as asthma, emphysema, edema of the lungs, etc. It is in the nature of respiratory function—alveolar respiration and pulmonary circulation—that these processes are so deeply hidden from observation, and even from the

possibility of satisfactory experimental investigation, and their integration must apparently remain forever largely a matter of intuition. Physiology and pathology offer one nothing but working theories. Why should the clinician not be permitted to offer his conclusions and working theories, based on his clinical experiences?

This venture in expounding my own evolved conceptions about these respiratory problems offers the only excuse, that it merely proposes to replace old assumptions by new ones. The only difference, as it appears to me, is that while the old assumptions raise new questions and run counter to one's clinical experiences, these new assumptions answer many questions and are congruent with the established clinical facts.

To present a problem of such dimensions in as brief a form as I intend to give here, I shall have to restrict myself to the mere outline of the ideas and the facts supporting them. Let them speak for themselves.

Every pulmonary disease, regardless of its etiology, presents the calcoscopy of decompensation and failure in some parts of the lungs with compensation of the other parts. My first task must be, therefore, to define the pathologic and clinical phenomena of decompensation and failure as well as those of compensation in pulmonary function. For this purpose I must go back to the basic conceptions of the physiologic and pathologic processes of respiratory function, after which I shall deal with the clinical features.

PHYSIOLOGIC CONSIDERATIONS

According to the up-to-date conceptions of respiratory function, breathing depends on the following mechanism. Inspiration is carried out by the activity of the external respiratory muscles under voluntary nervous control; expiration depends on the activity of the intrinsic muscles of the bronchi under vegetative nervous control. There is a prodigiously overprovided huge area of breathing surface, which undergoes little movement, but which is served by the supple systems of air and blood channels, so constructed that they can adapt themselves to a wide range of changes in respiratory requirements. Both the bronchi and the pulmonary arteries are endowed with the same elastic and smooth muscle structures, enabling them to undergo tremendous changes of capacity. According to the proportion of breathing surface in function and the intensity of this function, the wide range of variations in the capacity of the air and the blood passages is brought into play. These changes are precisely coordinated; they are always simultaneous and proportionate. With each inspiration both bronchi and arteries equally increase their capacity to receive the simultaneous increase of air and flow of blood brought to the lungs. The funda-

mental mechanism underlying normal respiratory function is this respirocirculatory correlation. Blood arrives in the lungs with a pressure so low that its circulation through the lesser circuit is maintained almost exclusively by the force of the pulmonary function of the respiratory excursions. Thus, air and blood in the lungs are promoted by the selfsame mechanism, the respiratory movements. It is a basic principle of pulmonary function that in any unit of the lungs there can be no circulation without ventilation, and that there can be no ventilation without circulation. With few limitations one can carry this principle still further and say that hyperventilation of a pulmonary unit means also its hypercirculation, while hypocirculation means also its hypoventilation. It is this precise correlation between ventilation and circulation that underlies the mechanism set in action with all variations in respiratory requirements. In exercise, increase of respiratory volume is parallel with increase in circulatory volume, while in sleep the opposite occurs. One must assume that this correlation is as precise in each unit of the lungs as it is in the whole of it. This correlation inherent in pulmonary function regulates the relation between pulmonary air and the blood depot from the first to the last breath. With the first breath of the infant, and closure of the botallian duct, a definitely correlated air and blood depot is established in the lungs, which is to be maintained to the last breath. The lungs, as the heart, never rest, and are never empty of blood or air. They are kept in constant expansion, under Donders' pressure, by the permanent presence of the air and the blood depot, which must ever be balanced to one another if function is to be maintained intact. Hence, there results the arrangement of residual air and blood volumes in the lungs, the air and blood depot, which are being constantly refreshed by the arrangement of tidal volumes of air and blood. The constant exchange of the pulmonary air and the blood depot is carried out by the same mechanism, the respiratory excursions, that coordinates the respirocirculatory correlation.

PATHOLOGIC CONSIDERATIONS

From the standpoint of functional pathology the most outstanding feature of respiratory function is the phenomenon of simultaneous compensation and decompensation present in the different parts of the same lung, or in the two lungs. Unlike the heart—an organ, all parts of which must stand or fail together—the lungs are a conglomeration of organ units, with a remarkable degree of functional independence. The units of the lungs behave independently and exactly like the whole of the lungs; they can fail separately, and can compensate one for the other. This situation permits a generalized discussion of respiratory failure, speaking from a purely functional standpoint. Whether decompensa-

tion or failure is local, restricted to a greater or lesser area of the lungs, or whether it is general, affecting the whole of the lungs, the pathologic sequence of events is the same. It will always depend on the interrelation of the failing and compensating areas of the lungs, of a restricted or general character.

As I have said, the foundation of normal respiratory function is the precise respirocirculatory correlation. This correlation is most precise when pulmonary function is kept at a mean standard. Diversions from the mean in respiration are fraught with upset in the correlation. Such an upset is equivalent to disturbed respiratory function, which may lead to respiratory decompensation or even failure. Accordingly, both extremes of hypofunction and hyperfunction are likely to lead to respiratory decompensation by way of upsetting the correlation between air and blood depot. Owing to this peculiar situation, one has the unusual opportunity in respiratory function, a phenomenon without its likeness in any other organic function, to be able to bring about respiratory decompensation at one's will. One can observe transitions from normal function to respiratory decompensation in normal persons by voluntary apnea and exhaustion from excessive exercise.

In voluntary apnea—Valsalva experiment—one sees phenomena threatening collapse of the lungs, if the experiment is carried too far. A depletion of the air depot and a marked increase of pulmonary blood depot, excessive pulmonary plethora, result. In lack of ventilation, transmission of blood through the lesser circuit drops far below the simultaneous reduction of blood supply. Even the reduced amounts of blood brought to the lungs under these circumstances are sufficient to bring about an excessive pulmonary plethora as compared with the reduced air depot, or state of pulmonary expansion. Hypofunction of any part of the lungs under a certain level produces such a local plethora, causing an engorgement. Patients with adequate circulation when immobilized in bed, so that expansion of pulmonary areas is markedly reduced, always develop such congestions. Any form of defective breathing, smothering or obstructed breathing is productive of such plethora. Hyporespiration, carried to the point of complete standstill for more than a few minutes, brings about such proportions of pulmonary plethora that alveolar capillaries become engorged. This also immobilizes the alveoli and interferes with their function, with the result that blood flow is still further reduced. Extreme engorgement of the alveolar capillaries follows, which changes the permeability of the tissues, permitting the transudation of blood serum into the tissues and air spaces. Atelectasis of the involved area of the lungs is thus produced. This is exactly what happens in complete occlusion of a bronchus, or the complete occlusion of the trachea.

The same result is produced in a somewhat different manner in hyperfunction that may be so excessive as to lead to pulmonary failure. The sequence of events is best illustrated in exhaustion from exercise, which is, paradoxically as that may sound, a physiologic form of respiratory decompensation. In excessive exercise the trained person has the ability of maintaining a precise correlation of excessively increased air and blood depot; not so, however, the untrained person. Such persons soon reach the limit of their ventilatory capacity, the greatest air and blood depot they can manage, beyond which they lose their power of correlation. In such persons, air and blood depot increased beyond a certain point become unmanageable, and the pulmonary emphysema and plethora, of a compensatory nature, become stagnant, because exchange must slow down. The reason for this slackening down of the turnover is, the slowing down prolongation of expiration, or expiratory dyspnea. It is a significant fact, that it is always expiration—depending on the activity of the intrinsic bronchial muscles under the control of the vegetative nervous system—that fails in respiratory function exceeding a certain level. The excessive pulmonary plethora and obstructive, stagnant emphysema thus produced are the phenomena of so-called respiratory decompensation. Carried beyond this point, hyperrespiration leads only to the further increase of pulmonary plethora, and finally to such capillary engorgement that pulmonary rigidity results. Capillary engorgement causes interference with alveolar function, and is the pathologic substrate of the clinical phenomenon one calls dyspnea. Pulmonary rigidity closes a vicious circle by which the lungs are completely immobilized; the circulation of the blood is severely handicapped, and the serum will leak into the tissues and air passages. Thus is pulmonary atelectasis produced by hyperfunction carried beyond a certain point.

Of course, normally the excessive dyspnea will stop men from carrying pulmonary plethora to the point of failure. However, instances of such fatalities in athletics that are carried to excess are described in the literature frequently. In excessive exercise, already at the point of considerable pulmonary plethora, people begin to cough and expectorate. Especially in dogs is the hacking and the emission of copious secretions from the lungs conspicuous. As a matter of fact, every pulmonary disease produces pulmonary plethora, hence the most outstanding feature of cough and expectoration in all of them.

The aforementioned mechanism by which respiratory failure arises in a quasi physiologic manner is also the mechanism by which it is produced in all pulmonary diseases, regardless of their particular pathogenesis. Hence, pulmonary atelectasis is of so variable a pathogenesis. Any disease of the lungs, whether its cause is mechanical, infectious or nervous, etc., leads to functional disturbance of greater

or smaller parts of the lungs and produces decompensation in some areas and compensation in other areas. The greater the failing area and the more severe it is, the greater must be the area of compensation or the more intense its hyperfunction. A struggle for predominance develops, on the outcome of which the final issue depends. The tendency will be on the part of the compensating area to help eliminate the failing part from function altogether. This is achieved by the "shunting" away of its blood supply and hastening its atelectasis and collapse by expanding at its expense. There are two good reasons for this tendency. First, if the blood supply of such an area of excessive plethora is maintained, and if the transudation of such large amounts of serum into the air spaces is kept up, the whole lung is threatened with overfilling. Such a condition was described by C. Jackson,⁵ who called it, "the drowning of the patient in his own secretions." Second, the compensatory areas of the lungs, by their hyperexpansion and hypercirculation, will encroach on the space and draw on the blood supply of the immobilized parts of the lungs.

This situation leads to the most interesting clinical and roentgen phenomenon of paradox excursions of the failing or decompensating areas of the lungs, as compared with those in hyperfunction. In massive collapse of one lung, as well as in obstructive emphysema—bronchial obstruction—in one lung, one sees the involved side expand in expiration, and retract in inspiration. The reason for this is that in inspiration the hyperfunctioning side expands at the expense of the involved side and "shunts" away its blood supply. In expiration, the involved side increases in volume and receives blood which is squeezed out again in the next inspiration. This explains the transmission of considerable volumes of blood through atelectatic lungs, and is responsible for the anoxemia produced under such circumstances.

The struggle for supremacy is conspicuous and clearcut only when decompensation and failure are on one side and compensation on the other side. When both failure and compensation are scattered over the whole of both lungs, the phenomena are more complex but essentially the same. The result is also the same.

In the clinical discussion one will see that this is really the underlying clinicopathologic phenomenon of all pulmonary diseases. Here one may conclude that failure in function of a lung area results in the production of excessive pulmonary plethora which finally floods the air passages and produces atelectasis. In short, the functional pathologic substrate of respiratory failure is pulmonary atelectasis. It amounts to stoppage of the circulation within the affected area, with the result that local edema is produced.

5. Jackson, C.: *Laryngoscope* 21:1183, 1911.

That this must be true for the whole of the lungs as it is for its parts follows from the well established principle that the whole of the lungs behave exactly as the parts do. The manner in which a local respiratory failure isolated to a part of the lungs can involve the whole of the lungs and produce general respiratory failure is obvious from the foregoing descriptions. Failure of one part must be compensated by hyperfunction in another part. If the failing area is comparatively small or failure is mild, compensation soon gains the upper hand and all is well. But, if the area failing is large, or if failure is intense, compensatory hyperfunction is likely to become so excessive that its advantages are exceeded by its grave dangers. If the area of compensation is limited, or if its hyperfunction is extremely intense, it will either "shunt" away too large blood volumes or bring about excessive hypercirculation, and will be fraught with an excess of pulmonary plethora. Excessive pulmonary plethora will, of course, lead to decompensation of the hyperfunctioning areas themselves.

One sees this happen frequently in all pulmonary diseases that reach critical stages. It is a common observation in massive collapse, obstructive emphysema or pneumonia, that the hyperfunctioning side is frequently more resilient in expiration than in inspiration. The reason for these phenomena is that under these circumstances excessive pulmonary plethora is produced in the hyperfunctioning side, which is actually a handicap to its efficient compensation. The fatal consequences of this situation are conspicuous in critical cases of pneumonia. Here the exaggerated compensatory effort gets the functioning areas of the lungs into serious trouble. Excessive plethora is produced of such proportions that the air passages of the uninvolved lungs are flooded. When the rattling in the good lung is first heard in critical stages of pneumonia it is the surest sign of approaching catastrophe, for it is the sign of oncoming general atelectasis and pulmonary edema. Thus pulmonary edema—diffuse pulmonary atelectasis—becomes the pathologic substrate of general respiratory failure. Lack of space does not permit me to go into a detailed discussion of the great pathologic puzzle of pulmonary edema. However, I want to call attention to the following two outstanding facts of experimental pathology. Producing a wide opening of the chest, or thoracotomy, is the surest way to bring about pulmonary edema in an animal; yet wide opening of the chest is also the surest way of saving an animal and of stopping pulmonary edema produced by injections of epinephrine. This paradoxical puzzle of experimental pathology on which endless experimentation has been done and on which the most copious literature has been written is explained in the light of my conceptions in a most obvious manner.

To open the chest of an animal widely means the crudest interference with its respiratory mechanism; the respirocirculatory correla-

tion is upset; the lungs will collapse; transmission of the blood depot is severely handicapped, the final outcome of which is excessive plethora and pulmonary edema. In the animal in which pulmonary edema has been produced by injections of epinephrine, or for that matter any pulmonary edema, tremendous pulmonary plethora is already present, and is being combated by compensatory emphysema of a degree which the animal is still capable of raising. In pulmonary edema the struggle between emphysema and atelectasis is extremely acute, because it is widely diffused over both lungs, and emphysematous expansion is greatly handicapped. If under these circumstances the chest is opened widely, that is, if thoracotomy is performed, emphysema gains room for its expansion, and can combat atelectasis successfully.

In pneumonia, asthma, emphysema and other conditions of the respiratory tract, pulmonary edema is the cause of death because there is no room for emphysema to effect the necessary compensation. In all these conditions, pulmonary edema is caused directly by respiratory failure. I believe I have presented sufficient evidence to show that pulmonary edema is the pathologic substrate of respiratory failure.

PATHOLOGIC ANATOMIC CONSIDERATIONS

The pathologic anatomic phase of the question of pulmonary atelectasis is at present in considerable confusion. This is due mainly to the fact that the interpretation of the term "atelectasis" is generally too rigid. There is fairly general agreement as to the application of the term to conditions in which actual shrinkage, or collapse, of lung volume is coupled with simple edema. This rigid interpretation of the term has somewhat relaxed with the recent progress in the recognition of atelectatic conditions. The term has recently been extended to include processes showing infectious or collateral edemas. Until lately, Coryllos and Birnbaum⁴ have advocated the application of the term to frank pneumonic processes.

Now the term "atelectasis" means lack of distention. There could be no more correct term for the condition. As has been shown in all pulmonary diseases, regardless of the etiology, immobility of the area of the lungs involved is the sole and paramount factor in the production of the changes. If one does not hold too rigidly to the restricted interpretation of atelectasis, the term will include every form of pathologic process of the lungs from collapse with simple edema, through all degrees of shrinkage of the pulmonary volume with transudation or exudation to infectious, collateral edemas and to pneumonia in which, though the volume of the lungs is augmented, airlessness and immobilization are complete. All of these conditions are based essentially on the same pathologic phenomenon, showing only different degrees of intensity. The outstanding features of all are: relative immobility to complete

fixation, lack of air to complete airlessness, emigration of blood elements into the air passages to their complete overfilling with these elements. All these conditions are forms of atelectasis of different quantitative degrees. The forms of atelectasis as found at autopsy show a wide range of variations as to the volume of the atelectatic lung and as to the morphologic elements which make up its histologic structure. The particular features of the different diseases, and even of the different cases, depend on the rapidity of the process. The more rapid the process becomes, the more complete the collapse and the less the edema. The slower the process is, the less the collapse, the more the edema and the greater the likelihood of the lung being invaded, even if the condition is not infectious in origin.

As a basis of discussion of pulmonary atelectasis, from the standpoint of its particular features, one should emphasize that the term "pulmonary collapse" should be restricted to the reversal of a fetal state of the lungs, namely, collapse of air spaces as well as vessels. Such collapse of the lungs is produced during life either by pneumothorax or by occlusion of a pulmonary artery. Any other form of pulmonary collapse is never a real collapse; it is "atelectasis." The degrees of atelectasis show great variations even in the same pulmonary processes of exactly the same etiology, and the anatomic features vary accordingly.

There is not the least dispute over the anatomic structure of the type of atelectasis which is generally understood by this term. All those describing its morphology, uniformly emphasize the lack of air and the marked dilatation of the pulmonary vessels, especially that of the capillaries which are filled with blood. The bronchioles are filled with serofibrinous exudate and frothy seromucous fluid. The pulmonary tissues are markedly edematous. The atelectatic lung shows different degrees of shrinkage, but is never collapsed to more than half of its original volume, frequently considerably less. The atelectatic lung is full of blood in its vascular bed and full of serum in its air passages. This explains its volume and weight. In short, the pathologic process in atelectasis is that of edema localized to greater or lesser areas of the lungs. In general edema of the lungs, collapse is usually even less than in partial edema, because compensatory areas are always present which hold a great deal of air in stagnant emphysema. However, the conception of complete airlessness in atelectasis is wrong. A part of the air depot is squeezed out of the atelectatic lung, but a great deal of the air remains and is dissolved in the fluid contents of the air passages; hence, the frothy foamy consistency of the contents of these air passages. The atelectatic lung even retains some degree of motility, as is evident from the roentgen observation of its paradox excursion during expiration. That the atelectatic lung still transmits considerable volumes of

blood is evident from the cyanosis present clinically. The amount of blood transmitted through an atelectatic area is also the index of the extent and intensity of the atelectasis. From the investigations of Andrus⁶ one knows that immediately after atelectasis the blocked lung still transmits about 30 per cent of the blood. From the investigations of Binger, Erich and Christie⁷ one learns that the circulation through pneumonic lungs is completely blocked, and that here atelectasis is therefore complete and immobilization and consolidation perfect.

Another form of atelectasis is that produced by infections. This, too, shows a wide range of variations from simple infectious edema to frank pneumonia. Here the question hinges on the age-old dispute of the differentiation between transudate and exudate. It is evident that the difficulty lies in the fact that there are no leaps in nature, transition is too smooth for sharp demarcations. Some pathologists make arbitrary delineations, and insist on sharp discrimination on the basis of morphologic features. Some authorities of international reputation say that they are at a loss when it comes to the drawing of a line of demarcation between simple and infectious edema of the lungs. In simple edema one finds exudation of fibrin, leukocytes and erythrocytes with desquamated epithelial cells. In infections, exudation frequently stops just at this point and does not go on to hepatization. The distention of the alveoli and compression of the blood vessels in inflammatory conditions contrast with the collapse of the alveoli and dilatation of the blood vessels in edema, but there are exceptions even to this. As Loeschke⁸ pointed out, in inflammatory conditions, too, one frequently finds the alveoli collapsed. The alveoli are distended by the coagulation of the exudate. In atelectasis, coagulation of the transudate does not usually take place, but even this may occur in atelectasis from bronchial obstruction, in which the air passages are so blocked that their contents cannot be discharged. In complete permanent occlusion of a bronchus, collapse does not take place until the coagulated transudate has been absorbed. Even in pneumonic processes, the first stage, before red hepatization, is just an excessive engorgement with edema. Even in frank lobar pneumonia the marginal areas are in a condition of simple collateral edema and atelectasis.

The relationship between atelectasis and inflammatory processes of the lungs has been defined in a most elucidating manner by Loeschke.⁸ This German pathologist, who has a great reputation, has described

6. Andrus, W. deW.: Cardiorespiratory Physiology Following Collapse of One Lung by Bronchial Ligation, *Arch. Surg.* **10**:505 (Jan.) 1925.

7. Binger, C. A. L.; Erich, W., and Christie, R. V.: *Klin. Wchnschr.* **7**:33, 1928.

8. Loeschke, H.: *Monatschr. f. Kinderh.* **41**:135, 1928.

inflammatory processes as hypertelestatic, dystelestatic and atelestatic conditions, to which differences he attaches pathogenetic significance. According to Loeschke, croupous pneumonia is hypertelestatic, the exudate is here primary in the alveoli, which are therefore found in distention. In bronchopneumonia, on the other hand, which begins in the terminal bronchioli, the air passages are blocked first; the alveoli are therefore partially or totally collapsed and one finds dystelestatic or atelestatic. The inference I draw from this is that in pneumonia the process is so severe that the entire area of the lungs becomes involved almost at once, and exudation is so excessive that it reaches all alveoli before they can collapse. In bronchopneumonia, a central area is first involved, and obstruction of air passages causes collapse of alveoli before the exudate can reach them.

The pathologic dispute over the line of demarcation between edema and inflammation is hottest in the question of the chronic localized edemas found at autopsy in patients who did not show any clinical signs of pulmonary disease. Prominent pathologists frequently diagnose such edemas as pneumonia. As a matter of fact, their frequently long duration predisposes to some infectious invasion, and the differentiation is then hopeless.

From this discussion one may safely conclude that the pathologic anatomic substrate of respiratory failure is atelestatic of the affected area of the lung. The pathologic anatomic substrate of all pulmonary diseases, regardless of etiology, is pulmonary atelestatic of variable degree and intensity.

CLINICAL CONSIDERATIONS

In a discussion of pulmonary atelestatic from the clinical standpoint, I should begin by pointing out that atelestatic is to some extent a physiologic condition. It is frequently observed over different areas of the lungs at examination of healthy persons. Even marked degrees of atelestatics may be observed, without clinical significance, in bed-ridden patients with competent circulation, if they are kept on their back for longer periods. Considerable degrees of atelestatic can be demonstrated in persons with markedly poor breathing by the tympany and râles which clear up after vigorous respiration.

Clinically, atelestatic shows a wide range of variations in degree, according to the pulmonary diseases but there is no disease of the lungs in which some degree of it could not be demonstrated. The most generalized forms of atelestatic are seen in acute suffocations, hanging, drowning and gassing. Massive total collapse is also a generalized form of atelestatic, which one should define as aborted pulmonary edema, the process being so abrupt that there is no time for frank edema to develop. Another generalized form of pulmonary atelestatic is present

in pulmonary anaphylaxis, in which the lungs are distended instead of collapsed because the process is so general, and in which the struggle between atelectasis and obstructive emphysema is so widely diffused that the fatal issue takes place even before the lungs could collapse. Another generalized form of pulmonary atelectasis is present in infectious congestions, the "fluxions" or the "fluxions poitrine" of the French clinicians. Milder types of generalized atelectasis are invariably present in miliary disseminations of infections, carcinoses and silicoses, in extensive pleural adhesions, emphysemas, diffuse bronchial processes (bronchiolitis) and other conditions.

Partial pulmonary atelectasis accompanies all local diseases of the lungs. I have observed it with great regularity in severe tuberculous lesions. It has been reported in pyogenic infections of the lungs. Recent investigations proved it to be the underlying factor of postoperative pulmonary complications. It is generally known as the outcome of all bronchial obstructions from foreign body aspiration or tumors, etc. Isolated patches of atelectasis are invariably seen about acute pulmonary lesions of whatever etiology. As such lesions never come to autopsy, the dispute is hot over their interpretation. Some call them perifocal inflammations, others think they are collateral edemas. Clinically, one frequently sees these areas disappear almost as abruptly as they came; when persistent, however, they may be infected and subsequently become a part of the lesion. As a rule the more severe the lesion, the greater is the atelectatic patch, and vice versa.

The mechanism producing atelectasis in all these clinical processes, regardless of their etiology, is, of course, the same. It is either failing respiratory function, by way of direct immobilization or by way of excessive compensation, which fails. The workings of this mechanism are plainly in evidence in all diseases of the lungs. The most clearcut picture of this mechanism is presented by the clinical entity of "massive collapse." In massive collapse, functional failure of greater or lesser areas of the lungs arises abruptly. There is a sudden closing down of ventilation at a time when considerable pulmonary plethora has been raised just previously. A respiratory crisis is precipitated, in which according to the severity of the condition greater or lesser areas of the lungs are abandoned to collapse, in order that the rest may take advantage of all available ventilatory capacity. The exact sequence of events is, of course, still a question that remains to be solved by future observations of the circumstances in which it arises. However, there are some suggestive points that should serve as points of departure for such investigations.

It is generally known that immediately after operations, especially under anesthesia, catarrhal phenomena are usually present in the lungs,

which betray the foregone plethora. The so-called "wet anesthetics" are merely more marked forms of this phenomenon. It is also a well known fact, that during most operations the patients hyperventilate, either because of the anesthesia or because of the anxiety. The pulmonary plethora is evident in the marked facial flush of these patients. In the presence of great pulmonary plethora, hyperventilation must be kept up on the top level, unfalteringly and steadily. Even the shortest interruption in ventilatory pace is most likely immediately to embarrass transmission of the large pulmonary blood depot. Reduction in ventilatory pace must be slow and gradual under such circumstances; otherwise it will precipitate a respiratory crisis. If under such circumstances wrong posture, smothering by covering of the face, abrupt increase of intensity of narcosis to the point of respiratory depression and other factors suddenly interfere with the ventilatory pace, respiratory failure of greater or lesser severity is produced. Under less severe conditions a timely compensatory effort saves the situation, preventing total collapse of the lungs by sacrificing some of the areas. Even under these circumstances all of the pulmonary areas are not involved to an equal extent. By abandoning to atelectatic collapse the most involved areas, the dangerous plethora is abducted through these areas, and the other areas have an opportunity to pick up in function. Probably, the leakage of serum is also the way by which dangerous plethora is reduced when respiratory excursions are so low as to fail to transmit the blood depot through the lesser circuit.

As to the bronchial plug theory of massive collapse, I think it is so untenable that it is not even worth discussion. I will, however, point out some of its inconsistencies for the sake of throwing some additional light on this interesting condition. As many workers have pointed out repeatedly, the most acute and fatal cases do not show any trace of a bronchial plug and are so abrupt that there could be no time for the absorption of the air; yet atelectasis is complete. Already Archibald⁹ raised the question, where does the vast amount of fluid come from if the bronchus is plugged? The question may be asked, where does the material which goes to make the plug come from? Bronchial obstruction causes only obstructive emphysema. In the animals in which it was thus possible to produce atelectasis, respiratory function was so impaired that the animals were incapable of normal response and could not raise any emphysema. The conception of absorption of the air behind the plug is all wrong. In the first place, the air passages in atelectasis contain a considerable amount of air dis-

⁹ Archibald, E. W.: Extrapleural Thoracoplasty in Treatment of Pulmonary Tuberculosis. *Arch. Surg.* **10**:328 (Jan.) 1925.

solved in the frothy foamy fluids, for what else could be the cause of this frothy foamy consistency of the bronchial contents? The conception of air absorption by the circulation is based on the experiments of Lichtheim¹⁰ who showed that atelectasis cannot be produced if, simultaneously with bronchial obstruction, the corresponding pulmonary artery is ligated. This experiment of Lichtheim does not prove that the air is absorbed by the circulation. As a matter of fact, the only thing this Lichtheim experiment does prove is just my contention that atelectasis depends on the production of excessive pulmonary plethora. What Lichtheim did by the simultaneous ligation of the pulmonary artery was the prevention of pulmonary plethora in the obstructed lung by cutting off its blood supply completely. Of course, this will prevent atelectasis, but not because the air cannot be absorbed. It was pointed out by workers repeatedly, and the scrutiny of the clinical features of massive collapse plainly show that the condition is a general respiratory distress affecting the entire lung; hence the frequency of multiple localizations. Could they all be plugged at once? To finish the discussion of massive collapse I shall point out, that while the condition is general, the great frequency of it in lower lobes, and especially that at the right side, is explained by the downflow of the bronchial contents, or transudations, into these lower parts of the lungs. This additional fluid accomplishes the drowning of these lobes much sooner than would take place otherwise. The same occurs in pulmonary hemorrhage.

The clinical presentation of pulmonary atelectasis—respiratory failure—must include at least a few remarks on the symptomatology. The physical signs of atelectasis show variations, from dull tympany to marked flatness; from the finest clicks to crepitation, rattles, and the peculiar suction sounds which were described by Williams (as quoted by Gairdner) as “clicking valve like sounds.” The roentgen phenomena also show a wide range of variations, from most intense opacity to just heavy cloudiness.

The subjective clinical phenomena of respiratory failure become manifest only when embarrassing proportions of the breathing surface or a severe form of ventilatory disturbance is affecting the lungs generally. The clinical symptoms of respiratory failure may arise acutely or develop in chronic progressive form. The cardinal symptoms of the “respiratory failure syndrome” are as follows:

1. Flush of the skin, especially that of face and neck, is frequently associated with chill. This flush I have found to be associated with the first phenomenon of respiratory failure, pulmonary plethora. In every condition in which pulmonary plethora exists I have invariably

10. Lichtheim, L.: Arch. f. exper. Path. u. Pharmakol. 10:54, 1878.

observed a facial flush. It is present in exercise exhaustion, in every acute pulmonary condition, from pneumonia and influenza, to massive collapse.

2. Dyspnea marks the degree of pulmonary plethora at which capillary engorgement has developed, and alveolar function is interfered with.

3. Cyanosis means transmission of unsaturated blood amounting to 6.7 per cent (Lundsgaard and van Slyke) of the total circulatory volume. It may be due to decreased ventilation or passage of blood through an atelectatic area.

4. Increases in the pulse and respiratory rate are phenomena of the compensation effort.

5. Cough and expectoration are due to the transudations into the tissues or even the air passages.

6. Cold sweats are probably due to a compensation effort for loss of pulmonary evaporating surface.

This symptom-complex takes on agonizing proportions in severe forms of respiratory failure. Under such circumstances circulatory decompensation phenomena become manifest, and the similarity to the condition of circulatory failure is great; hence, the traditional confusion of respiratory failure with circulatory failure. From the foregoing it is evident, however, that in respiratory failure it is pulmonary function that comes first to a stop. The circulation is then stopped short within the lesser circuit. Thus, death in respiratory failure is a genuine pulmonary failure, and not a cardiac failure.

THERAPEUTIC CONSIDERATIONS

I shall finish this discussion with remarks on the therapeutic side of the question. It should be emphasized here, that therapeutic results, when direct and clearcut, are the clinicians evidences to the correctness of his working theories and conclusions. They should be regarded as equivalent to experimental evidences. My contention that pulmonary atelectasis as it occurs in most pulmonary diseases is the pathologic substrate of respiratory failure is fully borne out by the results of all modern treatments for pulmonary diseases. Most of the methods are actually based on these principles.

To begin with, the most clearcut form of atelectasis is "massive collapse," and its prevention lies in obviating respiratory failure by artificial stimulation of respiration in form of inhalations of carbon dioxide. This is also the most successful treatment for this condition.

In a recent publication, Henderson and Haggard¹¹ recommended inhalations of carbon dioxide as a prophylactic measure against all pneumonic processes and as a procedure which has been found to be effective in all such conditions known to cause pneumonia, such as postoperative states, asphyxias from gas, etc. The effect of inhalations of carbon dioxide under such circumstances is the establishment and maintenance of ventilation adequate to the existing pulmonary plethora and assurance of the transmission of the accumulated volumes of blood.

In all critical stages of diseases of the lungs I employ artificial stimulation and support of respiratory function with oxygen inhalations. In conditions in which respiratory compensation effort is deficient, this method is helpful. Frequently, however, I have a situation in which overcompensation is the cause of a respiratory crisis, and in which stimulation is harmful. I see this conspicuously in the critical stages of pneumonia, in which the way of relief lies rather in depression of respiration, or reduction of pulmonary plethora. The salutary effect of morphine in just such critical pneumonias has always been a puzzle. The question has been investigated recently by Binger and Davis¹² by means of exact gas analyses carried out on a large number of patients with pneumonia. These workers concluded that "the benefits obtained from administration of morphine by way of relief of distress, reduction of metabolism, gain of sleep, outweigh the ill effects of reduction in ventilation, and increase of anoxemia." It is evident that in the critical stage of pneumonia the pulmonary plethora is to be combated even at the price of increasing anoxemia. My most excellent weapon in the combat against pulmonary plethora is bleeding. The effects of a copious phlebotomy in critical cases of pneumonia are frequently nothing short of miraculous. It is to be regretted that this powerful weapon of the therapeutic armamentarium of the fathers of medicine has gone out of fashion in modern medicine. Phlebotomy tackles the trouble at its root, and reduces venous return and with it also pulmonary plethora. Phlebotomy is the most effective treatment in a respiratory crisis of whatever etiology; it is the supreme treatment for pulmonary edema.

The modern methods of treatment for chronic diseases of the lungs have snatched the secret of nature; they are doing the same thing more effectively. As was shown in this discussion, the natural tendency is to eliminate the affected part from function. In the presence of extensive lesions, however, nature meets with insurmountable difficulties, and here is where one's methods come to the aid of nature and achieve collapse of the affected parts. The effect of these procedures lies in

11. Henderson, Yandell, and Haggard, H. W.: Hyperventilation of the Lungs as a Prophylactic Measure for Pneumonia, *J. A. M. A.* **92**:434 (Feb. 9) 1929.

12. Binger, C. A. L., and Davis, J. S., Jr.: *J. Clin. Investigation* **6**:171, 1928.

the additional room that is thus provided for compensatory expansion of the hyperfunctioning parts of the lungs. This is what saves the life of a patient whose great pleural effusion is aspirated. This effect is expressed in the tremendous extensions of lung volume of the functioning side in therapeutic pneumothorax, thoracoplasty, etc. The effect is also manifest in the failures of these procedures. Pneumothorax of too great pressure or a defective functioning lung that cannot take advantage of the opportunity for expansion offered are the causes of the failures. It is a well observed roentgen phenomenon in collapse therapy, that after each successive collapse the opacity of the functioning lung is increased at first. The reason for this is that after each collapse of the affected side, pulmonary plethora is produced in the unaffected side. But if pneumothorax pressure is not too high, and the lung is under no handicap (lesions or adhesions), the former resiliency is soon regained and even increased by further expansion and compensation. In pneumothorax work, this is the most reliable guide. Refilling should not be employed until the good lung has regained its former resiliency and production of collapse should cease when the functioning lung stops taking advantage of the opportunity for expansion offered. The respiratory failures arising after most successful surgical collapses are due to the failure of the functioning side to take advantage of the opportunity for expansion.

Compensatory expansion is the only way to combat respiratory failure. In all clinical conditions of respiratory failure, pulmonary edema is produced because of lack of compensatory expansion, either because there is not sufficient room or because there is not sufficient respiratory stimulus. Some patients with pneumonia die because they cannot effect sufficient respiratory compensation; others, because the solidified unyielding lung is in the way of proper compensatory expansion. The most clearcut evidence of this is the fact that even most desperate forms of respiratory failure may be successfully combated by the maintenance of respiratory expansions. Haven Emerson¹³ showed that persons with pulmonary edema may be successfully treated by artificial respiration, and he proposed this method for all forms of pulmonary edema in man.

CONCLUSIONS

All pulmonary diseases, regardless of their etiology—mechanical, infectious or nervous—produce respiratory failure, either localized in a restricted pulmonary area or general failure of the entire lung. The functional pathologic substrate of respiratory failure is pulmonary

13. Emerson, Haven: Artificial Respiration in the Treatment of Edema of the Lungs, *Arch. Int. Med.* 3:368 (May) 1909.

atelectasis. The pathologic anatomic substrate of respiratory failure is pulmonary edema.

The clinical substrate of respiratory failure is the "respiratory failure syndrome."

Death in respiratory failure is death caused by apnea. The circulation is stopped short within the lesser circuit.

CAVERNOUS HEMANGIOMA OF THE SCROTUM

REPORT OF A CASE*

NATHAN WINSLOW, M.D.

BALTIMORE

Cavernous hemangioma of the scrotum is a comparatively rare disease. Including Robert's case, described by Boullay, in 1851, I can find only ten cases listed in the literature. Of these, four were cited by Curling, as early as 1866, in the third edition of his monograph on diseases of the testis. Since then, as far as I am aware, no attempt has been made to consolidate the knowledge concerning this lesion. As I have recently had a patient with one of these neoplasms, it has occurred to me that a survey of the literature, with a brief history of my patient, should prove of interest, especially as modern textbooks give practically no consideration to the subject. Wyeth, in his "Text-Book of Surgery," disposed of the condition by saying that it occurs. Johnson, in his "Surgical Diagnosis," described a case, and Young, in his "Practice of Urology," said that two such cases were observed in his clinic at the Johns Hopkins Hospital, but he stated none of the details. All of the other books that I consulted did not mention the subject.

REPORT OF CASE

A white boy, aged 17, entered the hospital on Feb. 1, 1926, complaining of a lump in the right side of his scrotum which he had first noticed five months earlier, following a kick received while playing football. At that time the tumor was small; from the beginning, however, it grew slowly though steadily, until it attained the size of an orange. It had caused him no inconvenience other than a dragging sensation when he was on his feet. The growth was ovoid and reached above almost to the external abdominal ring, where it merged with the cord. The overlying skin was normal in color and healthy, but was thrown into corrugations by the underlying mass, to which it was lightly bound. A normal testicle could be distinctly felt at the bottom of the scrotum just behind the lower end of the swelling. The neoplasm gave the impression of being composed of a congeries of blood vessels, matted and intermingled in the utmost confusion. It was tender on pressure, and did not visibly decrease in volume when the patient lay on his back. It did not pulsate, and no bruit could be heard. The contents of the left scrotal sac were normal. While the picture was unusual, it bore no resemblance to that of a hernia, for which the boy had been sent to the hospital, or to a varicocele. As the patient had undergone seven operations at the Johns Hopkins Hospital for angiomas of the right leg, the first of which was performed four years and the last two years ago, this was thought to be a similar condition, and was diagnosed as such.

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Operation.—Operation was performed on February 2, with the patient under gas and ether anesthesia. The tumor was dissected out en masse through an incision 3 inches (7.6 cm.) long in the anterior surface of the scrotum. As soon as the subcutaneous tissues were reached, a conglomeration of dilated, tortuous veins and arterioles, incompletely surrounding the cord and testicle, came into view. Here and there vascular offshoots were sent into the skin. The bulk of the mass, however, was located beneath the skin. The tumor was supplied by two veins, located deep in the perineum, running in the groove between the rectum and the root of the penis. These were doubly tied and divided. The growth was



Cavernous hemangioma of the scrotum.

separated without much difficulty from the surrounding structures, and was removed. It was in no wise connected with the vessels of the cord.

Dr. W. J. Carson, at the time on the staff of the pathologic department of the University of Maryland, to whom the specimen was sent for microscopic examination, reported as follows: "Section shows the mass to be made up of a large number of dilated veins filled with red blood cells and a moderate number of arterioles, several of which contained organized thrombi." From this picture, he rendered a diagnosis of cavernous hemangioma of the scrotum with organized thrombi.

The postoperative course was uneventful, and the boy was discharged from the hospital on February 27 as cured. He was reexamined recently. The cure has persisted.

CASES CITED IN THE LITERATURE

Boullay described an erectile, subcutaneous neoplasm removed by Robert¹ from the scrotum of a man, aged 20, which had existed for twelve years. At the time of its onset the patient felt a sudden, abrupt pain in the right side of the scrotum, without known cause. Since that time his health had always been good, but the tumor had gradually increased in size. On the right side of the scrotum was an ovoid, bossellated mass. The skin was unchanged in color, but one could see beneath it a violaceous tint. No bruit could be detected. The cord and testicle were distinctly recognized. The excised mass consisted of dilated, erectile veins.

Ricord² described a case in a man, aged 29, who was admitted to the hospital on Nov. 20, 1855, with a tumor the size of the fist in the right side of the scrotum. It appeared to be congenital. When the patient was 11 years of age and again when he was 19, it became painful and inflamed without apparent cause. Nine years later, a third inflammatory crisis occurred. As the size of the tumor did not subside under treatment, the man decided to have it removed. The growth was ovoid and measured 20 cm. in length and 8 cm. in breadth. It extended up to the external inguinal ring and surrounded the right testicle and spermatic cord. The skin was not discolored. It was hard and did not fluctuate. There were no appreciable beats or bruit recognizable by the ear or by touch. Ricord could not recognize the cord or the testicle. He diagnosed the condition as an erectile, venous tumor of the scrotum, and on November 29, with the patient under chloroform anesthesia, he proceeded to enucleate and excise it. The man was discharged as cured on Jan. 5, 1856. A microscopic examination made by Verneuil showed the growth to be an erectile, vascular neoplasm which had undergone inflammatory changes. It contained a number of small cysts filled with a serosanguineous fluid.

Holmes³ reported the case of a boy, aged 10, who was admitted to the hospital on May 1, 1862, with a congenital, venous tumor of the scrotum. At first the growth had remained more or less stationary in size, but later it had increased decidedly; the growth was accompanied by the escape of blood from the urethra, though not in large quantities. The skin was intact and healthy over it, but it presented the venous color plainly. On palpation, numerous masses, more or less round and hard, could be felt. The cord could not be traced below the external ring, where it seemed to be lost in the mass. Nothing could be felt but a congeries of greatly enlarged veins. There was no pulsation. On the other side, the scrotum and testicle were healthy. A short time after the patient was admitted to the hospital, Dr. H. C. Johnson proceeded to operate by passing three ligatures as deeply as possible under the mass, and tying them tightly around the tumor and skin. This procedure diminished the bulk somewhat and appeared to have entirely checked its growth. On September 1, the boy was discharged as greatly benefited. After this operation, there was no recurrence of bleeding from the urethra. He was readmitted, however, on Jan. 20, 1863, when he was placed under Dr. Holmes' care. It was then thought best to place a ligature around the base of the tumor. Two needles were accordingly passed in, at right angles,

1. Robert, in Boullay: *Bull. Soc. anat. de Paris* 26:194, 1851.

2. Ricord, in Verneuil: *Note sur une variété rare et peu connue de tumeur des enveloppes scrotales; tumeur érectile veineuse congénitale développée dans le tissu cellulaire des bourses*, *Gaz. hebdomadaire de médecine* 6:581, 1859.

3. Holmes, T.: *Tumor of the Scrotum in a Boy*, *Tr. Path. Soc. Lond.* 15:95, 1863-1864.

through the base of the tumor, as deeply as possible, and an india rubber band was applied over them. This band gradually entered the scrotum to some distance, but did not divide the whole of the base of the swelling. The suppuration excited in the track of the needles was thought to have had considerable effect in consolidating the vessels at the base of the neoplasm. In July, 1864, there had been no fresh increase in the size of the growth. At that time, the testicle could be plainly felt lying at the top of the tumor.

Hewett⁴ mentioned having been called on to treat a patient who had a congenital, vascular tumor of the scrotum in which the arteries were universally enlarged, some of them being the size of the radial, and from which alarming hemorrhage had taken place. The growth was arrested and cure obtained by subcutaneous ligatures.

Rivington⁵ reported the case of a man, aged 23, who was admitted to the hospital on Jan. 16, 1875. A tumor larger than a hen's egg occupied the posterior part of the left side of the scrotum and extended into the perineum. Over the surface of the swelling, dilated veins were observed. To the touch, the tumor felt as if it was composed of enlarged veins mingled with little nodules of fibrous tissue scattered through it. At first the patient attributed it to a blow that he had received on the testicle a week before his admission. He said that he had never noticed a tumor in the scrotum before the injury, and that it had appeared suddenly after the blow and had not increased in size. According to the father, when the patient was 10 years of age he had received a blow in the same spot from his brother's knee; that the part had swelled, and that he had had leeches applied to the scrotum. Under this treatment the swelling subsided. The patient verified his father's statement, and said that the swelling had never wholly disappeared after the first injury. It seemed, therefore, most probable that the tumor was congenital, although it may have increased in size in consequence of the blows inflicted on it. On Jan. 28, 1875, the tumor was removed *en masse*, the surgeon making a longitudinal incision over it and dissecting it out. The cure was complete. Microscopic examination disclosed veins irregularly dilated. Small collections of fat and connective tissue were intermingled with the vessels. The structure was not that of an ordinary venous nevus.

King⁶ described the case of a white boy, aged 3 years and 3 months, with an enlargement in the left inguinal region which occurred suddenly and was accompanied by pain. He saw the patient on May 15, 1893, and three days thereafter, when the operation was performed, he thought the tumor had increased to twice its former proportions. The case presented all the symptoms of a left, complete, irreducible, inguinal hernia. A herniotomy incision revealed a venous mass knotted and twisted on itself; so much did it resemble an intestine that, had not the signs of strangulation been absent, it could easily have been mistaken for a gangrenous intestine. The dilatation of the vein began about one-half inch (1.27 cm.) to the left of the symphysis pubis and filled the left side of the scrotum. The convolutions were contracted to the size of a goose-quill at certain intervals and at other points dilated to the size of the little finger. The growth was found

4. Hewett, in discussion on Holmes: *Tr. Path. Soc. Lond.* 15:95, 1863-1864.

5. Rivington: *Vascular Tumor of the Scrotum; Removal; Recovery; Remarks*, *Lancet* 2:608, 1877.

6. King, G.: *An Uncommon Venous Tumor of the Scrotum*, *Alabama M. & S. Age* 7:238, 1894-1895.

to empty into a single vein. This was ligated. The entire mass was then removed. It had no connection with the spermatic vessels. The patient was permanently cured.

In 1908, Johnson⁷ removed a congenital cavernous angioma of the scrotum from a man, aged 26. The tumor had existed and grown steadily, though slowly, as long as the patient could remember. The mass of dilated veins and trabeculated blood spaces was as large as two fists when the patient stood erect. The venous channels communicated with two large veins running into the perineum in the angle between the bulb of the corpus spongiosum and the rectum. An illustration accompanying the article shows that the tumor was located on the left side.

Guardia⁸ reported the case of a man, aged 45, who entered the hospital complaining of a tumor in the testicle. Since birth he had had in the scrotum a "small dilated vein" which had never troubled him until five years ago. Eight months before, the mass had become large and tender, and on one occasion a profuse hemorrhage occurred. On examining the genitalia, one found a circular, spongy, purplish mass, involving the skin and extending over the whole left side of the scrotum and the upper posterior third of the thigh. It could be decreased in size and blanched on pressure. No expansile pulsation or bruit could be determined. The tumor was excised under spinal anesthesia. It extended well into the deep layers of the periurethral and perianal tissues. The mother veins were the internal pudendals. The man was completely cured.

Young⁹ furnished no detailed information concerning the two cases mentioned in his text. One he lists as case 7829. The patient was admitted to the Johns Hopkins Hospital for an angioma involving the scrotum, penis and the under surface of the thigh.

He dismissed the topic with the statement that hemangiomas in this region are rare venous varices, independent of varicocele, there having been only two cases in his clinic in which such varices involved the scrotum, penis and the under surface of the thigh. In the second instance,¹⁰ the case is registered as case 8231. The treatment employed in both cases, though Young did not say so, was apparently excision of the vascular tumor.

COMMENT

Of the aforementioned cases, only eight are described in sufficient detail for analytic purposes. These show a striking similarity in the method of their onset, development and symptomatology. In all, the disease began during the first or second decade of life as a small growth which gradually but steadily increased in volume to a size varying between that of a hen's egg (Rivington's case) and that of two fists (Johnson's patient). Occasionally the onset was abrupt, without known cause; at other times, the lesion was attributed to an injury. In none

7. Johnson, A. B.: *Angioma of the Scrotum*, Surgical Diagnosis, ed. 2, New York, D. Appleton & Company, 1911, vol. 2, p. 713.

8. Guardia, J. de la: *Cavernous Hemangioma of the Scrotum*, Fourteenth Annual Report, United Fruit Company, Medical Department, 1925, p. 137.

9. Young, H. H.: *Hemangioma of the Scrotum*, Practice of Urology, Philadelphia, W. B. Saunders Company, 1926, vol. 1, p. 711; see illustration on p. 470.

10. Young (footnote 9; see illustration on p. 479).

of the patients was the general health affected. In King's patient there was local pain, and in my patient a dragging sensation when he was on his feet. Examination revealed a tumor occupying either the right or the left half of the scrotum, with the overlying skin thrown into a series of hummocky folds. The skin itself, however, was healthy, intact and of a natural color, though the contained blood might be seen glimmering through it as a bluish streak. In every instance, the growth was confined almost entirely to the subcutaneous tissues and had no connection with the spermatic vessels. It was always unilateral. In none were beats or bruit felt or heard. The neoplasm was ovoid and more or less hard and lumpy. All of the patients were cured by operative measures, either by subcutaneous ligation, as in Holmes' and Hewett's cases, or by excision en masse. A remarkable feature of Holmes' case was the escape of blood by the urethra; this bleeding ceased after the first operation, never to recur. The growth showed no preference as to the side on which it appeared. Of seven cases in which this feature was mentioned, the tumor occurred in the right scrotal sac in three cases and in the left in four cases. The ages of the patients ranged from $3\frac{1}{4}$ to 45 years, respectively. Of more significance, however, was the age at which the tumor appeared.

Guardia considered tumors of this type as vascular new growths and not dilatations of already existing vessels, as suggested by Adami. Mallory regarded them as the product of endothelioblasts, and classified them as endotheliomas. He thought that the growth begins in the veins rather than in the capillaries, and at first takes the form of endothelial folds supported by a small amount of connective tissue, thus resembling the valves of the normal veins. As the tumor continues to grow, it becomes thrown into numerous folds which obstruct and dilate the vessels until their walls give way to pressure and permit the angioblastic mass to escape and invade the adjacent tissue.

The treatment is complete eradication of the growth by excision.

While a vascular tumor of this type in the scrotum is at most a comparatively minor ailment, I believe the infrequency of its occurrence at this site is sufficient justification for placing an example on permanent record and for calling attention to the few cases in the literature.

SURGICAL WOUNDS IN HUMAN BEINGS

A HISTOLOGIC STUDY OF HEALING WITH PRACTICAL APPLICATIONS : I. EPITHELIAL HEALING *

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Accurate knowledge of the process of epithelial repair in wounds is essential to a proper understanding of the clinical treatment of surfaces over which it is desirable to procure a covering of epithelium. In a recent histologic study of eighty-nine surgical wounds in all stages of healing in human beings, it was found that there are two distinct types of healing, epithelial and fibrous. Neither of these types falls directly into the existing descriptions of methods of tissue repair as taught in textbooks. As the two types of healing are distinct processes, and but little related to each other, they will be described separately. This paper will be confined to a description of the healing of epithelium, with clinical application of the observations.

An extensive review of the literature relating to epithelium in wounds and epithelium in tissue culture was made. Some basic facts concerning the potentialities of the individual epithelial cell were uncovered, the knowledge of which is important in arriving at a conception of epithelial healing: 1. The epithelial cell is potentially a motile cell, capable of progression over a suitable surface. It moves by means of pseudopodia.¹ It grows in tissue culture in continuous or branched membranes, the peripheral cells of which present pseudopodic processes. 2. The form of the epithelial cell in cultures depends directly on the type of base on which it rests. In fluid it becomes spherical, on a fiber it becomes stretched out and closely applied to the fiber. Stationary on a flat surface, it is round with a round nucleus, but in motion the same cell may become very long, flat and elliptical. All of these facts must be borne in mind in the interpretation of histologic pictures of epithelium.

The distinctive feature about epithelial healing is that it is a true outgrowth of new tissue from preexistent, functioning tissue of like kind. Vascular endothelium, alimentary epithelium and probably

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* Abridgment of thesis submitted to the Faculty of the Graduate School of the University of Minnesota, in partial fulfilment of the requirements for the degree of Master of Science in Surgery.

1. Fischer, A.: Tissue Culture, Copenhagen, Levin & Munksgaard, 1925, p. 107.

glandular structures apparently heal by means of the same type of process. Fibrous healing, on the other hand, takes place by the rapid production of a "fill" of new fibrous tissue between the severed portions of the preexisting fibrous structures, producing tissue union without true growth of new tissue from old tissue. Indeed, the term "growth" as applied to tissue is too loose a word to use with accuracy. It indicates only increase or enlargement without expressing the means of increase or enlargement.

The normal stratified squamous epithelium of the surface of the body is described in five layers; from without in (fig. 1) these are:

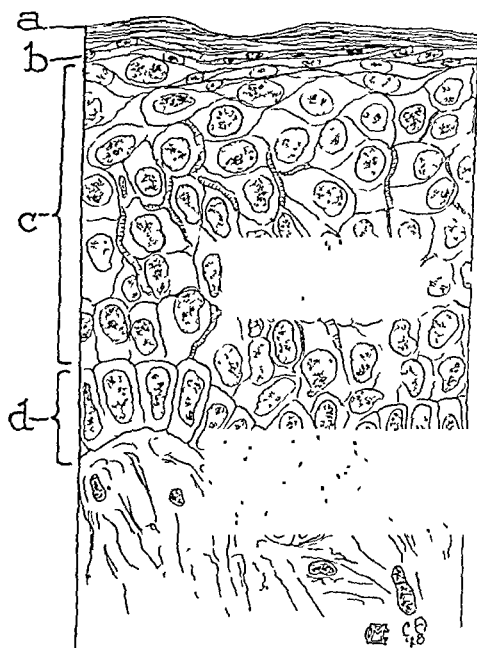


Fig. 1.—Normal human epithelium; *a*, cornified layer; *b*, granular layer; *c*, prickle cell layer, and *d*, basal cell layer; $\times 500$.

(1) cornified, or keratinized layer (dead cells); (2) stratum lucidum (rarely evident on other than palmar and plantar surfaces, composed of dead cells, and not considered in this paper); (3) granular layer (dead or dying cells); (4) prickle cell layer, malpighian layer or stratum mucosum (by some the lowermost cells are considered the germinal layers), and (5) basal cell layer, or palisade layer (more commonly accepted as the true germinal layer from which all other layers arise).

It is the basal cell layer which lies in contact with the dermis of the skin and which is considered to consist of the least differentiated

and most primary epithelial cells. The overlying layers, then, are formed by differentiation of the more embryonic basal cell in the process of keratinization. It is strongly suggested by the observations made in these human wounds that the primary epithelial cell is not the basal cell, but is the prickle cell of the mucosal or malpighian layer.

Although such a conclusion seems radically at variance with the present teachings of histology, in the literature there is considerable support for it. Loeb, in 1892, arrived at the same conclusion after studying experimental wounds in guinea-pigs, and he and his associates have since done much work to substantiate it. In fact, these observations in human beings correspond almost exactly with those described by Loeb² in guinea-pigs and later in the rat and the pigeon.³ As controls for these observations in human beings 101 wounds from one hour to fifteen days old were studied in guinea-pigs, rabbits, dogs and swine. The observations in the animals used as controls exactly paralleled those in human beings.

THE HEALING MEMBRANE

Grossly, about the margins of healing burns or ulcers there exists a thin membranous "outgrowth" of epithelium which lies on the denuded surface. In dry wounds this is usually adherent, but in wounds with considerable exudate it is possible to insert a thin instrument under this membrane and to lift it from its base. Such a "healing epithelial membrane" is found in all healing wounds, although its form may be greatly varied by local physical conditions, such as the type of surface it rests on and the amount of moisture in the wound. The mode of formation of this "healing membrane" and the factors influencing it are not generally understood and therefore bear description.

Perhaps the most common impression of the process of epithelial regeneration in healing of wounds is that, since the basal layer of the old epithelium is the regenerating layer, there occurs a rapid increase in mitotic division in the basal layer peripheral to the wound, which results in a large increase in epithelial cells about the margin of the wound. The new cells then get out in some way onto the surface of the wound as a direct extension of the surrounding basal layer. This primary basal layer then produces more cells which pile up above the basal layer to produce the normal prickle cell and granular and cornified layers of epithelium over the area of the wound. But this does not seem to be the process in human tissue.

2. Loeb, Leo: Ueber Regeneration des Epithels, Arch. f. Entwicklungsmechn. d. Organ. 6:297, 1898.

3. Loeb, Leo: A Comparative Study of the Mechanism of Wound Healing, I. Med. Research 41:247, 1920.

Special Structure.—In a wound one day old, the bordering epithelium will be found beginning to cover the cut ends of the incised dermis. This "extension membrane" is not formed by a lateral outgrowth of the basal cell layer. Instead, the upper cells of the prickle cell layer become elongated, they extend down over the cut ends of the other epithelial layers and the most distal cells lie directly on the exposed dermic fibers. The topmost cells become cornified, with the result that there appears to be an active extension directly into the wound of the uppermost prickle cell, granular and cornified layers. Such a condition is shown in figure 2.



Fig. 2.—First stage of epithelial extension into a wound one day old, in a human being. There is elongation of the upper prickle cells with extension over other epithelial cells onto the denuded dermis; the exposed cells are cornified and there is no outgrowth of a basal layer; $\times 700$.

By the time three days have passed, this extension of the epithelium may reach for a considerable distance over the denuded dermis; in figure 3 is shown a typical advancing epithelial membrane. Such a membrane is always closely applied to an underlying base. It is thinnest at the end most advanced into the wound and is as thick as the old epithelium where it arises from the old epithelium. At its point of origin it still appears to be a direct continuation of the upper layers of the old epithelium. Cornified material overlies it for most of its length. According to the usual criteria of form and staining qualities of

epithelial cells, the cells composing the membrane should be highly differentiated, squamous, pavement cells and they should be either dead or dying, like the granular cells of the old skin. Such a membrane, however, or some variation of it, is the only structure that is constant in wounds that are known to be healing. The cells that appear dead are therefore very much alive and active. The cells themselves are long and flat and stain darkly; their long rodlike nuclei stain very darkly. Aside from the shape of the cells in the membrane, the two most striking observations are that it appears to arise by an elongation and movement outward of the uppermost cells of the old

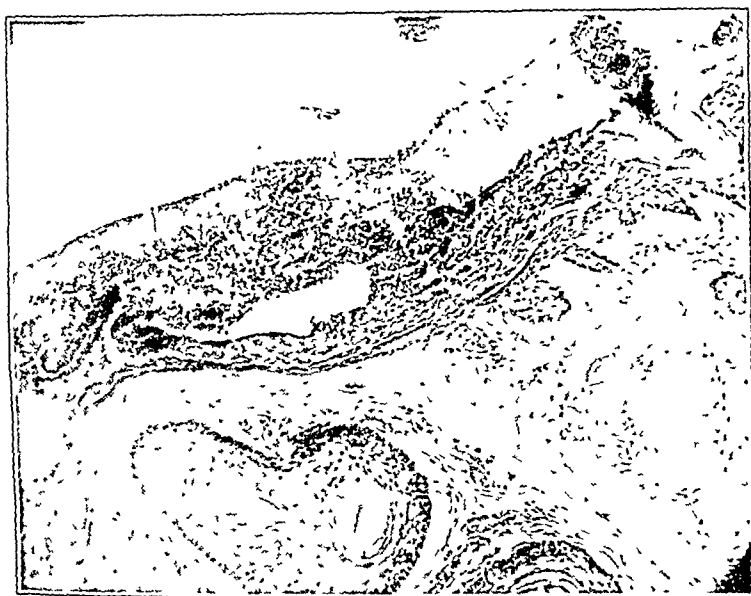


Fig. 3—Typical epithelial healing membrane on compact fibrous tissue in a wound three days old, in a human being. The membrane adheres to the underlying surface and is continuous with the upper cells in the old epithelium. There is no basal layer and cornified cells overlie the membrane. A thick layer of purulent debris overlies the epithelium; $\times 60$

epithelium, and that there is under it no semblance of a basal layer of cells. A third observation, namely, that mitotic figures are nowhere to be found either in the old or in the new epithelium, indicates that the membrane is formed by the preformed cells of the old epithelium which actually move out over the defect. Applying here the fact ascertained by tissue culture, that the shape of the cell depends on its supporting structure and rate of motion, the conclusion is reached that the long, flat appearance of the cells of the membrane is due to their being cells that are in active motion into the wound.

Such a conclusion is substantiated by the finding of rather typical, round, pale, epithelial cells clumped at the end of a membrane, or in depressions under it in places of evident stagnation. Such cells must arise from the long, flat membrane cells for they have no other means of arrival at their situations, nor any connection with the old epithelium than through the membrane itself. Even where such rounded cells pile up, as in the older portion of the membrane or in depressions under it, there may be no evidence of a basal layer. Thus, all the epithelial cells in the area of the wound arrive at their ultimate situations by means of their movement into the wound from the old

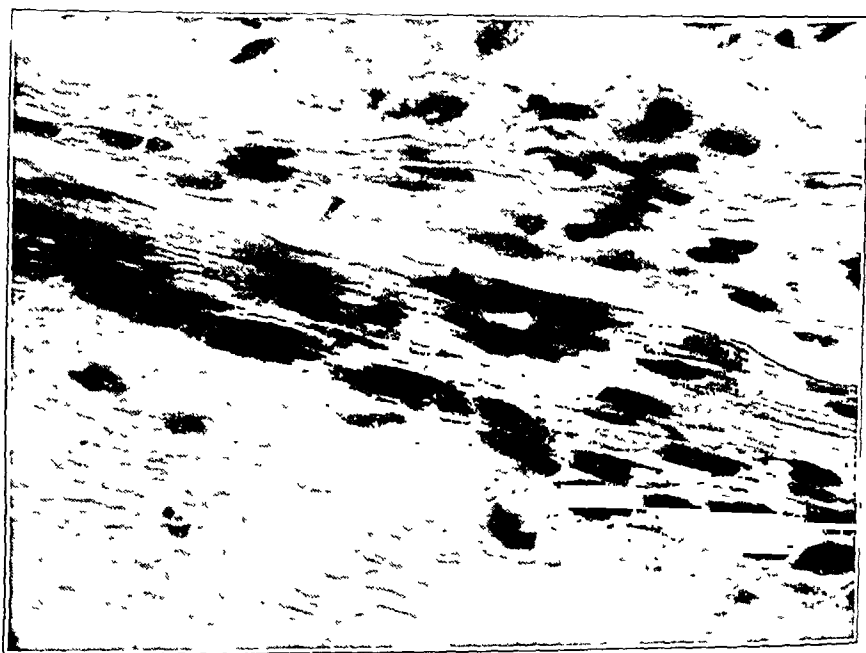


Fig. 4.—Higher magnification of section in figure 3, showing the typical appearance of cells of the membrane, the direction of axes of cells in the membrane, absence of a basal cell layer and cornified cells overlying the membrane. The membrane is advancing from right to left; $\times 900$.

epithelium, through the healing membrane. That this is so is shown also by the axes of the cells. In the old epithelium they overlap in a manner such that their axes point toward the membrane, whereas in the distal membrane the reverse is true; each cell next the dermis appears to have passed above the cells next nearest the old epithelium and then in turn to have come to rest itself on the fibrous base (fig. 4).

Origin of New Basal Layer.—A basal layer appears under the membrane late in the process of healing. The new basal cell layer

occurs in areas of cellular stagnation under the advancing membrane, where the deeper lying cells of the membrane have become rounded. This observation is of great interest. Since the cells in the membrane are derived chiefly from the preexistent cells of the upper layers of the old epithelium, and since the epithelial cells in the wound all are derived from such a source, unless a basal layer, as such, grows out from the old epithelium secondarily and under the membrane, whatever basal layer is formed under the new epithelium must be derived from the prickly cells of the old skin. There is no indication that there is at any time a true lateral extension of cells of the old basal layer other than that such cells may occasionally contribute to the formation of the membrane. Thus, the newly formed basal layer is derived from preformed prickly cells which have actively wandered into the denuded area. In the healing of wounds, therefore, the prickly cell must be considered the primary epithelial cell.

Occurrence of Mitosis.—After the wound is closed over with epithelium, or after about the fifth day, increasing numbers of mitotic figures may be found. The great majority of these are in the old epithelium, and they are by no means confined to the basal layer of the old epithelium. Likewise, under the older portions of the membrane, mitotic figures may be found in stagnant cells, but not in great numbers. Once the two membranes from opposite sides have united, the creation of the normal epithelial structure over the wound takes place by a continued increase of cells in the wound both by migration of cells from the borders of the wound and by local multiplication of cells.

The covering of a surface with epithelium is due, therefore, primarily to the motion of cells, and mitosis is of secondary importance in the essential process of covering the denuded area with epithelium.

Factors Influencing the Rate of Epithelial Outgrowth.—One characteristic of the epithelial membrane must be stressed. It always follows the available base. This in itself strongly points toward the extension of the membrane as due to ameboid motion, for it is inconceivable that cells move by themselves, without support. Tissue culture proves a base to be necessary for the motion of cells. If the cells were simply "juggled" out into the wound by tension existing in the old epithelium, or merely pushed out by rapid increase of their numbers, it would not be likely that they would always cling to the underlying structures as they do.

The tendency to follow the available base is so great that the membrane will advance in whatever direction the base leads, even though it lead directly away from the opposite side of the wound. Thus, every crevice and split in the underlying dermis or scar tissue becomes covered with epithelium and underlying spaces are prevented. If the membrane meets a mass of cellular or fibrinous debris which

offers several surfaces over which to advance, it will split and follow all of them. In this manner, eventually the tips of the two opposite membranes come in contact with each other over some surface, no matter how irregular, which extends from one epithelial margin to the other.

The type of base underlying the membrane appears to influence the form of the cells of the membrane and at the same time the rate of advance of the tip of the membrane into the wound. The membrane on compact fibrous tissue, such as that seen in figure 3, is



Fig. 5.—A typical epithelial membrane on a loosely compacted base in a wound three days old, in a human being. A short membrane and swollen cells are shown, and there is absence of a basal cell layer; $\times 80$.

long and thin, with long flat cells. If the advance is made over a poorly compacted base, whether dermis itself or "scab," the cells are less long and flat and the membrane as a whole is shorter (fig. 5). Fat tissue not covered with connective tissue fibers appears to be inimical to normal epithelial progression, for membranes on fat are very short and "swollen"; although two membranes are united over a short length of intervening fat, a basal layer does not appear even after seventy-three days.

The tendency of the epithelium to follow the available base leads to an interesting observation (fig. 6). In all of the wounds examined, the epithelium dipped directly into the incision over the cut ends of the dermis for a variable distance. This distance was determined chiefly by how much fat or new fibrous tissue was pushed up between the dermic ends from the subcutaneous tissues. As for any healing activity in the dermic ends themselves, there is none. They are inert.

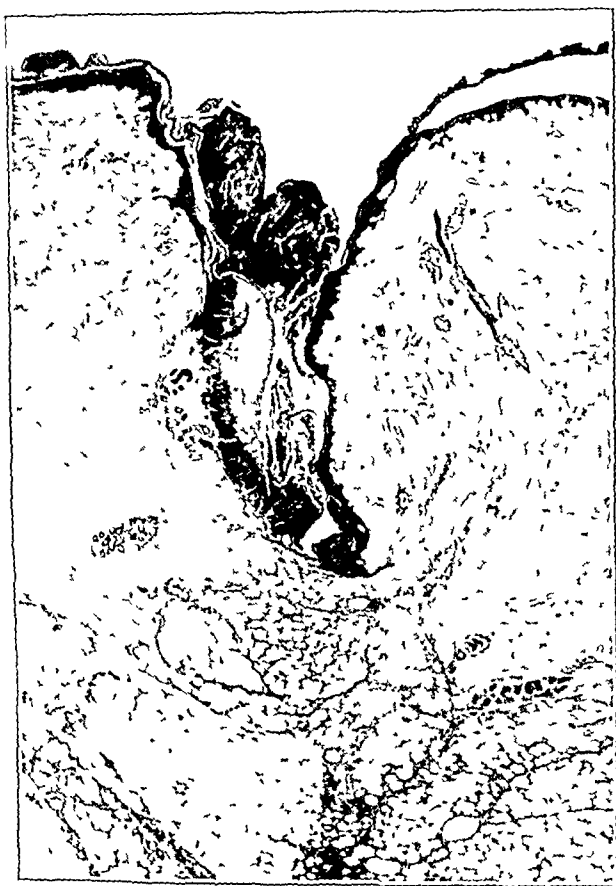


Fig 6—Transverse view of an apparently well healed incision ten days old, in human skin. The epithelium dips deeply into the incision, resting on the ends of the dermis, and the dermal ends are inert, $\times 18$.

From such observations it must be concluded that one of the chief factors determining the rate of advance of an epithelial membrane is the type of base over which the membrane must progress. Closely compacted fibrous tissue appears to be the optimal base. Fat is the least favorable base.

Curiously enough, cornified material (fig. 4) overlies all but the most recent portions of the advancing membrane, giving the appearance of active extension of the cornified layer of the old epithelium into the wound. Such an active function for a dead structure is inconceivable. The more probable explanation is that cornification is related to the exposure of cells and the resultant cellular death. As the cells form the membrane, the topmost cells become exposed, with the result that they die and become cornified. The accretion of newly exposed cells at the terminal end of the cornified layer thus produces the appearance of active extension of the cornified layer into the wound.

From these observations another factor determining the rate of epithelial advance can be derived. Cornification or hardening of the exposed cells follows the advance of the membrane. This process demands the death of the cell, and this promptly removes the cell from those moving into the defect. If the amount of cornification is increased,

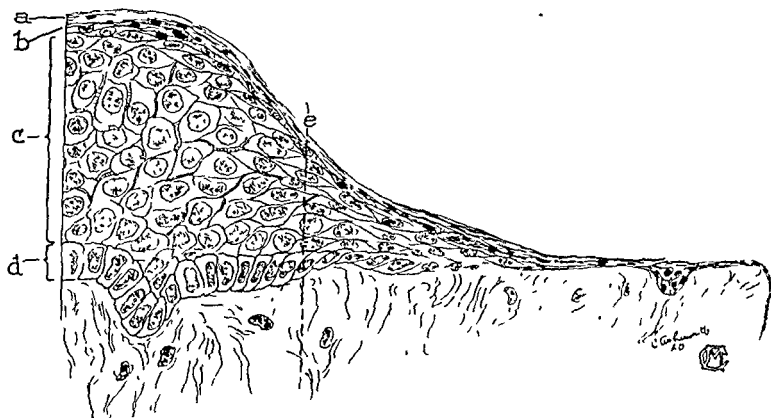


Fig. 7.—The mode of formation of the healing epithelial membrane in wounds of human beings. The drawing shows the origin of membrane cells from prickle cells, cornification of the topmost or exposed membrane cells, producing a direct continuation of cornification into the wound, rounding up of cells in stagnant areas under the membrane and the membrane following the available base. *a* indicates cornified layer; *b*, granular layer, *c*, prickle cell layer; *d*, basal cell layer, and *e*, point of incision.

it is obvious that the rate of advance of the membrane must suffer. The rate of cornification of the cells of the membrane, therefore, must be considered an important factor in the rate of epithelial outgrowth. Figure 7 is a diagram of the healing membrane, showing its various characteristics.

CLINICAL APPLICATIONS

The two factors which determine the rate of epithelial advance are susceptible to variation by clinical treatment. Indeed these two

factors must be the basis of many well established clinical precepts of the management of wounds which have been arrived at empirically. In the first place, infected wounds are known to obtain their covering of epithelium more slowly than clean wounds. Under the microscope, three conditions obtain in infected wounds in greatly exaggerated degree: 1. There is an increased number of cornified cells overlying the healing epithelial membrane. 2. There is likely to be loose granulation tissue, presenting a greatly increased surface to be covered by the advancing membrane, with the additional hazard of many deep clefts which must be filled with stagnant cells of the membrane before the membrane can proceed in its further advance into the wound proper. 3. There is likely to be much loosely compacted wound débris, over or through which the branches of the membrane will grow, only to be lost when the débris sloughs off or is torn off in the dressing of the wound, or over which the normal epithelial layered arrangement does not take place. At once, the actual effect of infection on the epithelium in a wound becomes translated into the two factors which determine the rate of the process of covering with epithelium; these are the rate of cornification of the advancing cells and the material and structure of the base presenting for the support of the advancing membrane.

From such a correlation of clinical and histologic observations, it must be assumed that the best way to hasten the process of covering with epithelium is to secure in a wound conditions the chemistry and physics of which provide the least amount of exposure inimical to the continued life of the advancing cells of the membrane, thus reducing the rate of cornification in the membrane, and to provide a suitable base for the epithelium to adhere to and to move on. It is probable that all wound dressings have their good or ill effect according as they fulfil such requirements. Any increased rate of healing after treatment is due to the reduction of conditions inimical to the epithelial advance, thus permitting the epithelium to "grow" at its optimal rate.

There is nothing new in the suggestion that the type of base determines successful epithelial outgrowth. In skin grafting with Reverdin or Thiersch grafts it always has been stressed that the base must clinically be "clean and healthy," and free from infection, and fluid must not be allowed to collect between the epithelium and the base. Moist dressings are carefully applied so as to reduce to a minimum the amount of exposure of the healing cells.

Again, it is doubtful that anything so drastic as the application of the cautery to the edge of a delicate epithelial membrane is actually stimulating to the cells of that membrane. Cauterization coagulates the accumulated serum and the loosely grouped granulations, thus providing in another manner a suitable, compact base for epithelial

progression. Various methods of applying pressure and protection, such as adhesive tape, petrolatum, gauze, sponges, etc., all fulfil the same ends.

Thus, the benefit, if any, of any particular method of wound dressing may be looked for in its action toward procuring: (1) a satisfactory base for the epithelium to wander out on, and (2) physical and chemical protection for the cells of the membrane against an inimical environment which would cause increased cornification of the healing cells.

As Mills⁴ has said concerning this work, it "has much to do with the histogenesis of epithelial tumors of the skin." Later, Dr. Mills intends to publish the results of his investigation in this field.

CONCLUSIONS

1. The living cells of normal human epithelium are potentially ameboid cells.

2. In the healing of wounds covering with epithelium takes place through the ameboid movement into the wound of cells from the surrounding epithelium. Such moving cells form an "extension membrane." The process of covering with epithelium is completed by the union of two such membranes from opposite sides of the wound, followed by the rearrangement and multiplication of the cells of the membrane.

3. Mitosis occurs secondarily to cellular movement and late in the process of healing.

4. The majority of the cells which form the extension membrane are derived from the prickle cell layer of the old epithelium.

5. A basal cell layer is formed under the epithelial outgrowth by a rounding up and alinement of the lowermost cells of the membrane, rather than by outgrowth of cells from the old basal layer.

6. The prickle cell of the normal epithelium is therefore capable of becoming the basal cell in the epithelium of the scar and must be considered the primary cell in the regeneration of epithelium in the healing of wounds.

7. The formation of the healing epithelial membrane is dependent on a supporting base suitable for the movement of epithelial cells.

8. The base available for the support and advance of the epithelial membrane is the chief factor determining the time and place of the union of the epithelium from the two sides of the wound.

9. The rate of cornification of cells of the membrane is also a determining factor in the rate of the process of covering with epithelium.

4. Mills, R. C.: Discussion, Proc. Staff Meetings Mayo Clinic 3:247, 1928.

10. The chief causes of delayed epithelial healing, therefore, are the existence of a supporting wound surface unsuitable for progression of epithelial cells, and rapid cornification of the cells of the membrane due to inimical chemical or physical environment. The conditions just named are accentuated in infected wounds.

11. Any beneficial effect of a particular method of dressing wounds may be referred to its action toward producing a more suitable base or more suitable environment in which the epithelial cells may grow out normally.

PRIMARY CARCINOMA OF THE FALLOPIAN TUBE

A SERIES OF FOURTEEN CASES *

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The present study is based on a series of fourteen cases of primary carcinoma of the fallopian tube. This is, we believe, the largest series that has yet been studied in any one clinic. Five of the patients were in the Johns Hopkins Hospital; the remainder were operated on in neighboring hospitals, all but two by members of our staff, and the operative specimens were brought to this hospital for study. Seven of these cases have already been reported at various times by Hurdon,¹ Vest² and Cullen.³ In order to bring the series down to date and complete it, the entire group has been included and studied in this summary. It is fortunate that we have been able to obtain fairly complete clinical and pathologic data and follow-up records in every case.

FREQUENCY

Primary carcinoma of the fallopian tube is one of the rarest of gynecologic conditions. In 1925, Liang⁴ collected reports of 214 cases from the entire medical literature. Since that time, additional cases

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1. Hurdon, Elizabeth: A Case of Primary Adenocarcinoma of the Fallopian Tube, *Bull. Johns Hopkins Hosp.* **12**:315 (Oct.) 1901.

2. Vest, Cecil W.: A Clinical Study of Primary Carcinoma of the Fallopian Tube, *Bull. Johns Hopkins Hosp.* **25**:305 (Oct.) 1914. *Malignant Growths in the Fallopian Tube*, in Lewis, Dean: *Practice of Surgery*, Hagerstown, Md., Prior Publishing Co., 1928, vol. 11, chapter 25.

3. Cullen, Thomas S.: Carcinoma of the Right Fallopian Tube Readily Palpable through the Abdomen, *Bull. Johns Hopkins Hosp.* **22**:20 (Jan) 1911; *Primary Carcinoma of the Right Fallopian Tube*, *ibid.* **16**:397 (Dec.) 1905.

4. Liang, Zue: Was lehrt das primäre tubencarcinom in pathologischer Hinsicht? *Virchows Arch. f. path. Anat.* **259**:577, 1926.

have been reported by Barrows⁵ (3), Covarrubias⁶ (1), Heil⁷ (1), Kurtz⁸ (1), Bower and Clark⁹ (1), Vest² (1), Callahan¹⁰ (1), Bültemann¹¹ (1), Kittler¹² (1), Cameron¹³ (2), Stanca¹⁴ (1) and Scott and Oliver¹⁵ (2), a total of 16 cases. Including all, there are probably not more than 230 cases on record.

It is interesting to compare the incidence of primary tubal cancer with that of other gynecologic diseases. In the Johns Hopkins Hospital, for example, in 35,000 patients with gynecologic conditions there have been only 5 cases. In 1927, Barrows⁵ stated that there had been only 3 cases in a series of 30,000 patients with gynecologic conditions treated in the Bellevue Hospital of New York. S. J. Cameron¹³ of Glasgow remarked in 1925 that primary carcinoma of the fallopian tube was such a rare condition that many gynecologists had never encountered it.

RACIAL PREDISPOSITION AND AGE

Liang brought forward the observation that of 214 cases, reports of which he had collected, 107 occurred in Germany, 26 in France, 23 in England, 13 in Austria, 8 in Hungary, 6 in Russia, 5 in America and the remainder in various other European countries. It is difficult to believe that this observation has any significance as far as racial susceptibility is concerned; we rather think that it merely indicates the relative regularity with which gynecologists and pathologists in various

5. Barrows, D. N.: Primary Carcinoma of the Fallopian Tube, with Report of Three Cases, *Am. J. Obst. & Gynec.* **13**:710, 1927.

6. Covarrubias, P. Alvaro, and Albertz, Arturo: Carcinoma de la trompa de fallopio (Case), *Bol. Soc. de cir. de Chile* **4**:188, 1926.

7. Heil, K.: Primäres tubenkarzinom, *Zentralbl. f. Gynäk.* **50**:2952, 1926.

8. Kurtz, H.: Fall von einem einseitigen primären tubenkarzinom ausgezeichnet durch das Vorhandensein zahlreicher riesenzellähnlicher Gebilde, *Ztschr. f. Geburtsh. u. Gynäk.* **90**:133, 1926.

9. Bower, J. O., and Clark, J. H.: Primary Bilateral Carcinoma of the Fallopian Tubes; Recognition of Early Metastasis Essential to Successful Treatment; Report of a Case, *Arch. Surg.* **11**:586 (Oct.) 1925.

10. Callahan, W. P.; Schlitz, B. A., and Hellwig, A.: Primary Carcinoma of the Fallopian Tubes Associated with Tuberculosis, *Surg. Gynec. Obst.* **48**:14 (Jan.) 1929.

11. Bültemann, H.: Primary Cancer of the Fallopian Tubes, *Zentralbl. f. Gynäk.* **51**:1037, 1927.

12. Kittler, E.: Primäres tubenkarzinom mit impmetastase auf dem endometrium, *Zentralbl. f. Gynäk.* **51**:971, 1927.

13. Cameron, S. J.: Malignant Disease of the Ovaries and Fallopian Tubes, *Brit. M. J.* **2**:285, 1925.

14. Stanca, Constantine: Primary Cancer of the Fallopian Tube, *Gaz. d. hóp.* **100**:1155 (Aug. 31) 1927.

15. Scott, E., and Oliver, M.: Primary Carcinoma of the Fallopian Tubes, *J. Lab. & Clin. Med.* **14**:429 (Feb.) 1929.

countries record their unusual cases. Since 1925, 6 new cases have been reported in Germany and 14 (including the present series) in America.

The age incidence is about the same as it is for carcinoma in general, most of the cases occurring between the ages of 40 and 60. One case was observed in a woman, aged 70, and one in a woman of 25 (Bower and Clark⁹).

PREDISPOSING FACTORS

Salpingitis.—In 1895, Säger and Barth stated that primary carcinoma of the fallopian tube had its origin in the irritation produced by chronic salpingitis, and since that time much evidence has been advanced to support or refute this supposition. The proponents of this theory point to the fact that in a large number of cases there are definite signs of chronic tubal inflammation. Thus, in one of the cases that we are reporting (31798), it is certain that the patient had had salpingitis for at least four years, undoubtedly of gonorrheal origin. Four of our fourteen patients had salpingitis at the time of operation. Cameron recalled the unusual coincidence of pyosalpinx and cancer in a patient operated on by Lawson Tait.

It is impossible, however, to determine the number of cases in which salpingitis has preceded the development of carcinoma, not only because of the lack of detailed histories in the recorded cases, but also because the tumor itself may produce a chronic inflammatory reaction, which, according to Doran,¹⁶ may close the tube and simulate hydrosalpinx. Although four of our cases showed tubal inflammation at the time of operation, in only one were we certain that the salpingitis was an independent process which had antedated the development of malignant disease. The relationship between cancer and tuberculosis is even more remote, for only six cases are on record in which these conditions existed simultaneously in the fallopian tube. Even if in every case it could be demonstrated that tubal cancer had been preceded by chronic salpingitis, one could hardly draw any definite conclusions because of the extreme disparity in the frequency of the two diseases, cancer being the rarest and salpingitis the commonest of tubal diseases. After careful study of all of the recorded cases, Wechsler,¹⁷ Vest and also Liang apparently hesitate to accept the opinion of Barth and Säger. It seems to us, also, that one would hardly be justified in assuming that salpingitis plays any notable rôle as a precancerous lesion, although it is impossible to deny that chronic irritation may precede malignant metaplasia.

There is, however, another side to the question. For if chronic salpingitis may possibly be an unfavorable factor which predisposes

16. Doran, Alban: A Table of Over Fifty Complete Cases of Primary Cancer of the Fallopian Tube, *J. Obst. & Gynec. Brit. Emp.* 6:285 (Oct.) 1904.

17. Wechsler, H. F.: Primary Carcinoma of the Fallopian Tubes, *Arch. Path.* 2:161 (Aug.) 1926.

toward cancer, it also plays the favorable rôle of setting up an effective temporary barrier against the early dissemination of the malignant growth by closing the tubal ostium.

When the tube is sealed, the growth may assume enormous proportions and many months may pass before it breaks through the tubal walls. On the contrary, if the tube is open, bits of the cancer escape into the peritoneal cavity early in the course of the disease, and this dissemination soon causes death. Furthermore, the pressure of the fluid and the tumor in closed tubes causes sharp pain and forces the patient to seek medical assistance quickly; when the tube is open, however, there may be no definite symptoms until the abdomen begins to enlarge because of ascites and peritoneal metastasis. Hence, we feel that in such cases salpingitis may prove to be a blessing, though considerably disguised.

It is interesting to contrast the uterine and tubal epithelium as regards other factors that might be concerned in the development of cancer in view of its frequency in the one and its rarity in the other organ. Both tissues arise from the mullerian ducts. The uterine epithelium is extremely active and is always in a state of menstrual transition; it undergoes tremendous hypertrophy during pregnancy and is exposed to injury and trauma much more frequently than is the tubal mucosa. Moreover, there are three different types of uterine mucosa, and it is well known that carcinoma seems to have a tendency to develop at points where two types of epithelium meet. In contrast, the tubal epithelium is remarkably inactive and is well protected. Although it exhibits cyclic changes corresponding with the menstrual phenomena, they are slight. There is no recurring monthly desquamation and regeneration, and even during pregnancy the tubal mucosa alters little. Consequently, these circumstances produce a situation which offers scant opportunity for cellular overgrowth, hyperplasia or unusual cytologic activity. Whether or not these factors are of any consequence is merely a conjecture.

PATHOLOGY

Sänger and Barth divided primary tubal carcinoma into two types, papillary and papillo-alveolar, and this classification has been generally quoted. Friedenheim added a third, the alveolar wall type. In 1925, Liang made a careful pathologic study of the subject and arrived at the conclusion that the various types which Sängér, Barth and Friedenheim¹⁸ had suggested were only stages of one process and did not represent real morphologic differences. He consequently contended that their classification was arbitrary and unnecessary. It is quite certain that in our

18. Friedenheim, Bernhard: Beitrag zur Lehre vom Tubencarcinom; Ueber ein primäres rein alveolares Carcinom des Tubenwand, Berl. klin. Wchnschr. 36:542 (June 19) 1899.

cases one can find all of the foregoing types represented, except the "alveolar wall" type of Friedenheim, which we have never seen. In almost every individual growth, moreover, there are areas that are distinctly papillary, others alveolar and others solid. On the basis of the cases we have studied, we agree with Liang that fundamentally the tumors are identical histologically, exhibiting only such minor varieties in growth and morphology as one would naturally expect. Furthermore, we have been able to offer no differentiation as to grades of malignancy, judging either from the histology of the growth or the clinical end-result. Although it may be true that some tumors are largely alveolar and others papillary, there is at present no evidence that they are inherently distinct or that their behavior is different in regard to malignancy, methods of extension or clinical characteristics. This phase of the subject merits further study as new series are reported.

The lesion is usually situated in the middle or outer third of the fallopian tube. Depending on the size of the growth and the patency of the fimbriated extremity, the gross appearance of the tube varies. If the abdominal ostium is closed, the tube may present every appearance of a hydrosalpinx, except that it is often bluish or purple, because of the dark color of the enclosed fluid. A coexistent salpingitis, pyosalpinx or tubo-ovarian cyst may completely mask the situation. The tube is often adherent. On opening it, one finds the pale, papillary growths of variable size. Some of them are attached by such slender pedicles that they break off and float out with the dark, coffee-colored fluid. When the tubal ostium is open, these masses may be clearly visible at the fimbriated extremity. In such cases, one usually finds peritoneal metastases and at times ascites.

The neoplasm has its origin in the mucous membrane of the tube. Various stages of metaplasia may be observed in any one case. In some areas the tubal epithelium is markedly hyperplastic, and small papillary growths replace the fine wavy tufts of normal mucosa. In these papillae, there is little connective tissue framework, the growth consisting chiefly of single layers of tubal epithelium, arranged in glandlike pattern, suggesting the picture found in adenocarcinoma of the endometrium. The epithelial cells themselves show no abnormal change, but the pattern shows malignant disease.

In other papillae in which the process is further advanced, there is a heaping up of the epithelium so that it may be several layers thick or may even form solid nests of cells. The cells become more and more irregular in shape and atypical, and the nuclei are hyperchromatic. One could entertain no doubt as to the presence of a malignant condition in these papillae.

As the papillae enlarge and press against each other, they unite to form solid masses of tissue. The alveoli are filled with a hyaline secre-

tion, and the papillae tend to lose their individuality. Mitotic figures, lymphocytic infiltration and occasional areas of necrosis appear. This stage corresponds with the so-called papillo-alveolar type.

In primary carcinoma, the tubal growth is predominantly inward, toward the tubal lumen, and the masses usually fill the tube and distend it before there is the slightest tendency to invade the muscularis. This was the situation in all of our cases. In one, reported by Cullen, the tube formed a large cystic mass that reached the umbilicus and was filled with fluid and carcinoma (fig. 2); yet, in spite of the size of the growth, the tubal wall was everywhere intact, although it was so stretched that it was only 2 or 3 mm. thick. In advanced cases, the tumor may invade the adjacent tubal wall superficially; as a rule, however, metastases occur elsewhere long before that happens (figs. 1, 2, 3, 4 and 10). This is, indeed, a most striking phenomenon and has led some observers to doubt the malignancy of the tumor; a casual perusal of the end-results, however, even in apparently hopeful cases, discredits any such supposition.

Carcinoma of the tube is often bilateral. In 183 cases, Wechsler found the growth on the right side in 64, on the left in 62 and bilateral in 57. There are, moreover, various indications which suggest that both tubes are involved more often than we suppose. In some cases in which the growth is apparently unilateral (Liang 2 cases and Wharton and Krock, 1), there is a suspicious papillary hyperplasia of the mucosa in the supposedly sound tube; furthermore, in some cases in which unilateral salpingectomy has been done, early recurrences have been observed in the tubes which looked normal and were not removed. In view of the established fact that the growth is often bilateral, both tubes should always be removed.

Metastasis occurs early and is widespread because of the many means of ready dissemination. When the tubal orifice is open, peritoneal implants occur early, and the disease rapidly reaches its fatal termination. When the fimbriated extremity is closed, the growth may remain limited to the tubal mucosa for months and eventually spread by direct extension to the mesosalpinx, the adherent ovary, the uterus and peritoneum or be carried to more distant organs by the lymphatics or the blood stream. Rarely, as in one of our cases (34,144), are implants observed in the endometrium; when diagnostic curettage has been done in such cases, the pathologist's report on the curettings has been adenocarcinoma of the body of the uterus, a correct but somewhat incomplete verdict. Implants are prone to occur in the abdominal scar or in the vaginal drainage tract. The pelvis is rich in lymphatics, and metastases have been observed in the inguinal, lumbar, sacral, hypogastric and external iliac glands. Rossinski reported an instance in which the

supraclavicular glands were involved. Secondary growths have also been noted in the liver and mammary glands.

It is interesting to compare primary with secondary tubal carcinoma, for they are unlike in every particular. Secondary cancer is more common than primary. It usually comes from the ovary, cervix or endometrium, and the picture of each is characteristic. In ovarian cancer, the growth may be by direct extension or by peritoneal or vascular dissemination. In carcinoma of the cervix, we have observed that the growth reaches the tube by the lymphatics, and that one finds small islands of typical squamous cancer in the tubal wall or mesosalpinx. In endometrial carcinoma, the tube may act as a channel for the transmis-

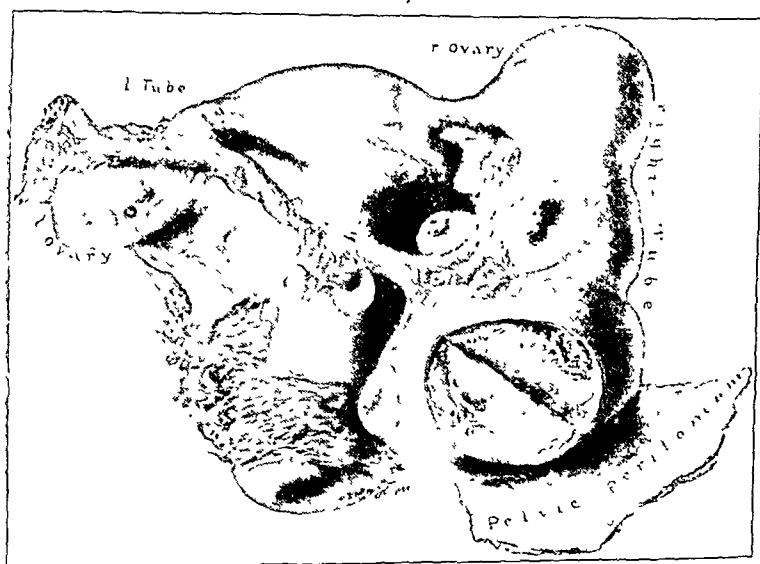


Fig. 1 (no. 8114).—Primary carcinoma of the right fallopian tube. The external resemblance to pyosalpinx should be noted. Carcinoma was recognized at operation, however, and an extremely wide dissection made (panhysterectomy, removal of six inches of bowel and adjacent pelvic peritoneum); recurrence and death in six months. (From Bull. Johns Hopkins Hosp., by courtesy of Dr. Thomas Cullen).

sion of malignant cells, as Sampson¹⁹ has shown. In such cases, one finds the malignant tissue loose in the tubal cavity. It is conceivable that it might become fixed and grow on the tubal mucosa, although we have not yet observed this. None of these secondary tubal growths have the branching, treelike characteristics of primary cancer, nor do

19. Sampson, John A.: Peritoneal Endometriosis Due to the Menstrual Dissemination of Endometrial Tissue into the Peritoneal Cavity, *Am. J. Obst. & Gynec.* 14:422 (Oct.) 1927.

they share its other manifestations. The striking difference between primary and secondary tubal carcinoma is the fact that primary cancer almost never invades the tubal wall, whereas secondary growths almost always start there.



Fig. 2 (no. 11536).—Unusual case of primary carcinoma of the tube, reaching almost to the umbilicus. The tube wall is not invaded, even by a growth of this size. (From Bull. Johns Hopkins Hosp., by courtesy of Dr. Thomas Cullen).

THE CLINICAL PICTURE

It is hardly remarkable that no one has yet diagnosed primary tubal carcinoma before operation; indeed, in the vast majority of instances,

the condition has escaped recognition, even on the operating table. When the tube is closed, adherent, cystic and enlarged, the diagnosis of hydrosalpinx or pyosalpinx has been made. When it is evident that a malignant process is present, the diagnosis has usually been ovarian cancer or peritoneal or pelvic carcinosis. Although in some cases surgeons have recorded that the tube had unusual or peculiar characteristics, in few instances has it been stated that the diagnosis was made unqualifiedly without the aid of the microscope. Many times the malignant fallopian tube has been overlooked entirely, so intent has the operator been in removing a benign myoma or ovarian cyst. The gross appearance of the tube may certainly be most deceiving, but it is our impression that usually the correct pathologic diagnosis could be reached if the tube were opened and examined in the operating room. This might also have some bearing on the surgical treatment and possibly on the end-result.

The earliest and most constant symptom of primary carcinoma of the fallopian tube is pain. Vaginal discharges of various sorts—watery, purulent, leukorrheal or sanguineous—then appear. Menstrual disturbances, malaise, weakness, fever, dysuria, gastro-intestinal symptoms, abdominal enlargement and cachexia develop as the disease progresses.

Pain is the earliest symptom and is usually definite and severe. In this respect, carcinoma of the fallopian tube gives a danger signal much sooner than almost any other intraperitoneal malignant lesion. The pain is sharp and colicky, is usually located in the iliac fossae, and may be accompanied by nausea and vomiting. At times, it is sudden in onset. In many instances the sharp pain is superimposed on a dull pelvic discomfort which may have been present for years, due perhaps to pre-existent salpingitis, ovarian cyst, injury at childbirth or myoma. The sharp pain recurs frequently for months, with increasing severity as the disease progresses.

The early onset of pain is probably due to the tension produced by the increasing secretion of fluid and the growing tumor within the closed tube. At times, pain is a late phenomenon, and then the earliest symptom may be an unusual vaginal discharge or abdominal enlargement due to ascites.

Vaginal discharge may appear early in the course of the disease. Almost every variety of discharge has been noted, the usual type being a watery or leukorrheal, blood-tinged fluid which is persistent. Foul-smelling, green, yellow and brown discharges have also been observed.

Because of such vaginal discharges in patients within the cancer age, curettage has frequently been performed. At times, polyps, myomas and benign endometrial changes are present to confuse the picture; under these circumstances, the persistence of the discharge after the correction of the uterine condition is extremely significant, and should direct one's attention to the adnexa. If curettage reveals no pathologic

endometrial change in a woman who has a sanguineous watery discharge, one should think of tubal carcinoma, particularly if other symptoms are present. Under these circumstances, the presence of an adnexal tumor is an indication for laparotomy.

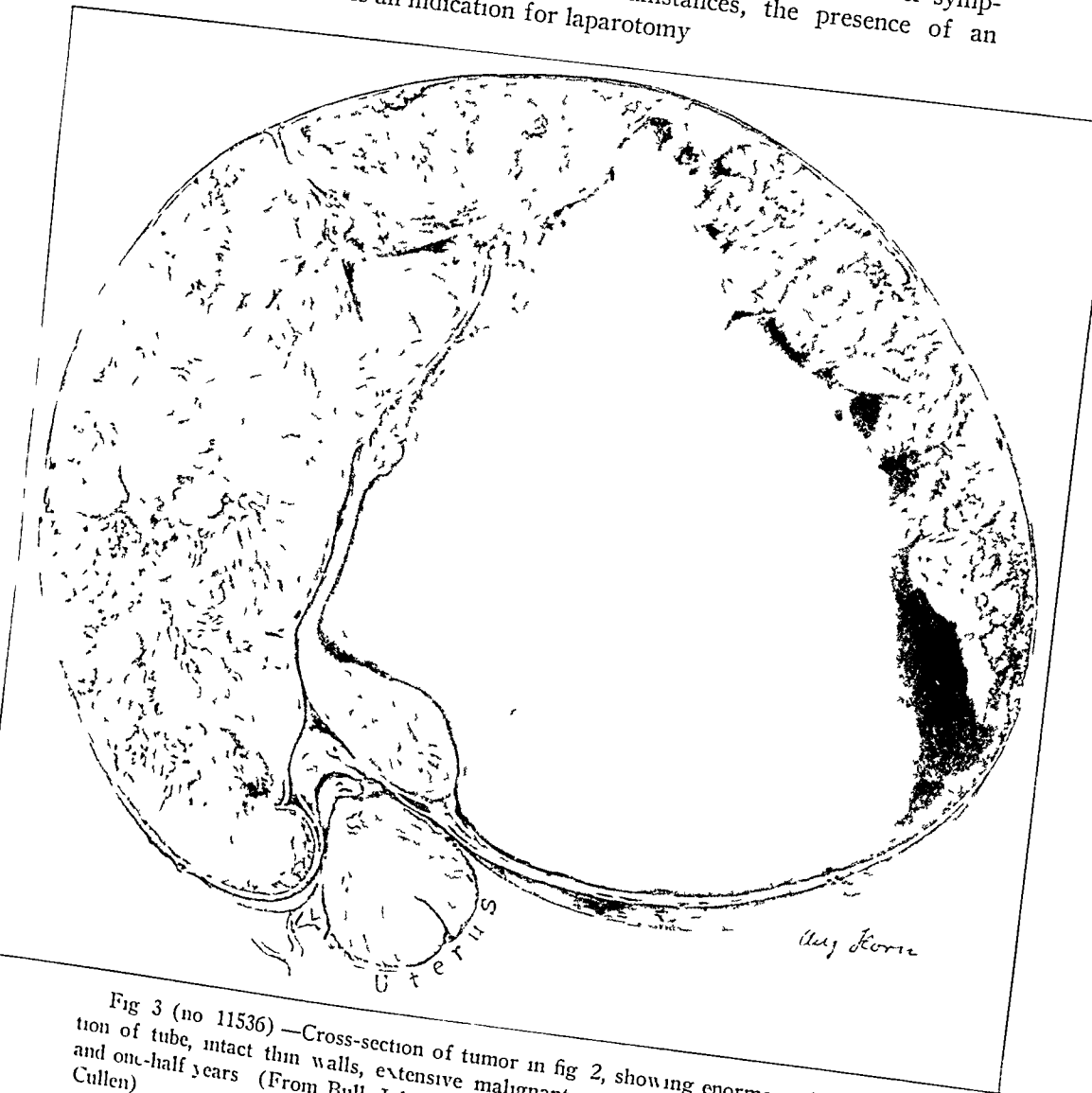


Fig 3 (no 11536) —Cross-section of tumor in fig 2, showing enormous dilatation of tube, intact thin walls, extensive malignant growth, recurrence in three and one-half years (From Bull Johns Hopkins Hosp, by courtesy of Dr Thomas Cullen)

The amount of fluid that may be discharged per vaginam is amazing, in one instance being about a liter a day. Wechsler noted that the discharge may be periodic and may be accompanied by paroxysmal pelvic cramps which diminish or cease after the fluid escapes. In these cases,

the situation is apparently analogous to *hydrops tubae profluens*, in which the tubal secretions escape through the uterus into the vagina. Since in the majority of these instances the uterine epithelium is normal, one must suppose that the discharge has its source in the tube.

When the fimbriated extremity of the tube is open, the secretions carrying bits of carcinoma escape into the peritoneal cavity. Under such conditions peritoneal metastases appear early, and ascites may be the first symptom. It is noteworthy that the sharp colicky pain which usually forces surgical intervention may not be felt in cases in which the fallopian tube is patent.

Practically all patients with tubal carcinoma have an abnormal vaginal discharge.

The menses are often affected by the disease, and almost every type of menstrual irregularity has been observed. It is quite probable that at times the menstrual disturbances are attributable to coexistent conditions, such as myomas, salpingitis, menopause and ovarian cysts. In many instances, menstruation has not been disturbed.

The usual menstrual irregularities are menorrhagia and metrorrhagia, although temporary amenorrhea has been noted. Because of the menstrual irregularity, pain and adnexal tumor, tubal pregnancy has often been suspected, although the age of the patient frequently excludes this possibility. Intermenstrual bleeding may be profuse, but this is not the rule. Dysmenorrhea may or may not be present. Taken as a whole, the menstrual phenomena are variable and give little assistance in elucidating the situation.

Backache is rather common, as it is in all pelvic disorders.

Gastro-intestinal symptoms, while not uncommon, are not as prominent as those which have been enumerated. Nausea, vomiting, constipation and pain on defecation have been observed, and in the advanced states, abdominal swellings and masses occur.

Urinary symptoms may be marked. In one case (Amann), the only complaints were referred to the bladder. At times incontinence appears, without any metastatic lesion in the bladder or urethra. As a rule, however, dysuria, frequency and other urinary symptoms form a relatively minor part of the syndrome.

Contrary to the opinions of many observers, sterility has not been prominent in our cases. It has been repeatedly stated that sterility is common in women who subsequently develop tubal cancer, and this has been advanced to support the contention that salpingitis precedes the development of malignant disease. This is not our experience.

A glance at our summary shows that of the twelve women who were married, nine had conceived, the total number of pregnancies being forty-one. Of the fourteen miscarriages, all but two were admitted to have been induced. Only three patients had not conceived; of these, one

married after the age of 40, one contracted salpingitis immediately after marriage and in the third, the cause of the sterility through twenty-three years of married life was not explained. In this case, there was no salpingitis at the time of operation and the tubes were open. In these twelve cases, therefore, there were only two definite cases of sterility, and in only one of these was it due to salpingitis. In our experience, therefore, sterility is not a feature of these cases, and salpingitis is known to have preceded the carcinoma only once. In the majority, the child-bearing function has been essentially normal, in spite of the fact that three patients had myomas and one a large ovarian cyst. In this series there were two instances of "one child marriages," in one case apparently because of a large fibroid and in the other because of the development of an ovarian cyst.

PHYSICAL OBSERVATIONS

One is surprised at the lack of uniformity in the conditions found at pelvic examination. In the clearcut simple case, there is a solitary adnexal mass of variable size, which is usually soft, fixed and tender. At times this mass may be hard and may occupy the culdesac of Douglas; in a few instances, the tumor shows fluctuation. In advanced cases, the tubal mass fills the lower part of the abdomen and is accompanied by ascites. Glandular enlargement is present at times.

When the condition is complicated by myomas, ovarian cyst and pelvic infection, as it often is, the symptoms are immediately obscured, and the diagnosis becomes practically impossible. When, as has happened, obesity and local tenderness make it impossible to feel any tumor, one can be guided only by one's clinical judgment and by the process of elimination. In such cases, the association of lancinating, persistent pelvic pain with a blood-tinged vaginal discharge should suggest the presence of a definite pelvic disease which requires surgical exploration. This is particularly true if the patient is in the carcinoma age and previous curettage has revealed nothing.

One would have to search long to find a medical or surgical condition that has eluded diagnostic skill as completely as has tubal carcinoma, for there is only one observer who has claimed that he even thought of the correct diagnosis before operation. The reason for this is to be found in the extreme rarity of the condition and the absence of any characteristic signs.

We can conceive, however, of certain conditions under which one would be justified in making the diagnosis tentatively. The development of a profuse, blood-tinged vaginal discharge in a woman beyond the menopause immediately suggests carcinoma of the uterus. If by palpation and curettage the uterus is found normal, if there has been severe pelvic pain and if one can feel an adnexal mass, tubal carcinoma

should be considered as a possibility, although one must also think of neoplasms of the ovary and salpingitis, particularly tuberculous.

In younger women, the diagnosis is *much more difficult*, because of the great number of tubal, ovarian and uterine lesions that can produce the same symptoms. As a rule, however, the discharge is more profuse than in other adnexal conditions; the mass is usually softer than a pyosalpinx or ovarian neoplasm, and the history goes back farther than it does in ectopic pregnancy.

The difficulty of making the correct diagnosis is almost always magnified by the presence of other pelvic lesions. Some patients have been treated conservatively for acute salpingitis and pelvic peritonitis; they may have had these and may have been discharged from hospitals when they were convalescent, only to find that they had tubal carcinoma when abdominal section was performed later. Except in *uncomplicated* cases, we doubt seriously whether in the child-bearing period the disease can be diagnosed with certainty *before operation*, because of its *extreme* rarity and the protean character of its symptoms. In older women, the chance of accurate recognition is greater.

Even on the operating table, the disease has often eluded recognition. In many a case, the operator has performed a conservative unilateral salpingectomy and has closed the abdomen, believing that he has removed a pus tube. At times, the presence of malignant disease has not been suspected until the report from the pathologic laboratory has been received after the patient has left the hospital.

In most cases, the simple expedient of opening the fallopian tube in the operating room would probably establish the diagnosis.

TREATMENT

The only treatment which has proved successful has been surgical. The ideal treatment would be removal of both tubes, ovaries and the uterus by block dissection, giving as wide a margin to the growth as possible. Since both tubes are frequently involved, since metastases occur in the endometrium and because of the proximity of the ovaries, it is *unwise* to attempt to save any of these organs. The only hope lies in complete and early extirpation.

Radiotherapy has been tried in a few cases, usually with poor results. Bültmann (1927) irradiated a patient, aged 50 years, for one and one-half years under the impression that the bleeding and pelvic pain were due to carcinoma of the uterine body. This treatment apparently had no effect on the course of the disease. Postoperative irradiation has been employed at times, usually in hopeless situations, without benefit. As Burnam said, the condition is so rare that few radiologists have had occasion to treat it; hence, for the time being, this phase of the subject remains an open question.

If one were to base his prognosis entirely on the results of the past, it would be necessary to conclude that the outlook is almost hopeless. In 1926, Wechsler found only 6 three-year cures in about 200 cases.

In our series of fourteen cases, three patients have lived three, four and five years, respectively. Of these, one died apparently without recurrence five years after the operation; the second was well at the end of four years, and the third was well after three years had elapsed. Nine patients, however, died of recurrence, one four years after the operation. Two patients have not been observed long enough to warrant conclusions. It is obvious that these results are not satisfactory.

The high mortality seems to be due to several factors—the extreme malignancy of the tumor, late operation and incomplete operation.

Primary carcinoma of the fallopian tube is a highly malignant growth. The disease rapidly reaches the inoperable stage if the tubal ostium is open and peritoneal implantations occur. When dissemination is prevented by the closed fimbriated extremity, however, the growth may remain circumscribed for months or even a year or more, if one may measure the duration of the disease by the clinical symptoms.

Although the dismal surgical results of the past are due in large measure to the extreme malignancy of the growth, it seems to us that we should survey the situation carefully in the hope of discovering some way in which it might be improved. We are impressed by two other facts—first, that surgical intervention has often been tardy, and second, that the operative procedures have frequently been extremely conservative.

The delay in intervention is in many cases the result of the patient's procrastination. Frequently, however, the delay has been prolonged by the surgeon who little suspects that he is dealing with cancer, but believes that he is treating with commendable conservatism a benign inflammatory process. It must be remembered that in not a single instance has the correct diagnosis been made unreservedly before operation, although in many the presence of malignant disease has been suspected.

The large number of recurrences is also due in some measure to the conservative operation that has been done, for hysterectomy with removal of both tubes and ovaries has been performed in less than one third of all reported cases. In the remainder, the operative procedures have been variable—removal of part of one tube, unilateral salpingectomy, unilateral salpingo-oophorectomy, bilateral salpingo-oophorectomy and others. Since the tubal disease is often bilateral and may involve the uterus and ovaries, it is apparent that conservatism is futile.

It is quite probable that the surgical treatment would have been more uniformly radical if the operators had suspected the presence of a highly malignant disease. This situation could readily be corrected by the gross inspection of the tube in the operating room.

REPORT OF CASE

History.—Mrs. A. B., a housewife, aged 29, admitted to the Women's Hospital in November, 1926, had had excellent general health until the age of 16, when she was operated on for appendicitis and peritonitis. Following this, there was no abdominal discomfort until after marriage, in 1922. After this, recurring attacks of discomfort developed in the suprapubic region, associated with painful and

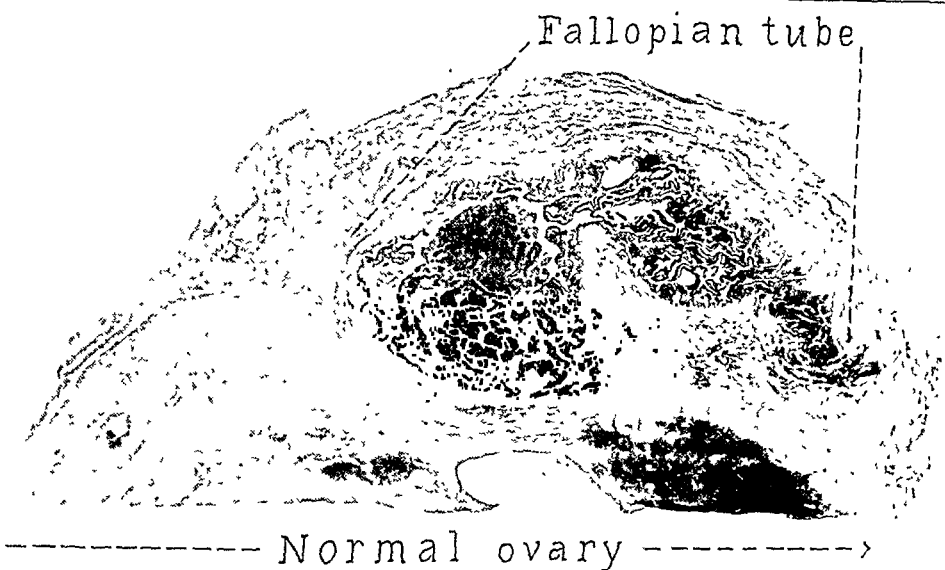


Fig. 4 (no. 31798).—Cross-section through the left tube and ovary; tubal lumen filled with carcinoma; no extension into muscularis or ovary; $\times 5$.

frequent urination. There was no nausea or vomiting. During the last three or four months, the pain had become sharp and paroxysmal and localized in the left iliac fossa. Between these sharp attacks, there was a continual dull pelvic discomfort.

The patient had always had some leukorrhea, even as a young girl. Recently this had become profuse and malodorous, but never bloody or irritating.

Menstruation began at the age of 13. Until the past year, the interval had always been twenty-eight days, the flow lasting four or five. During the past year, the interval had been three weeks, without any other variation from the usual cycle. There had been no intermenstrual bleeding or menorrhagia. The menses were occasionally painful, but never excessively so.

Physical Examination.—The patient looked healthy and was well nourished; the skin was clear and the mucous membranes were a normal color. General medical examination gave negative results.

The abdominal examination gave negative results, except for distinct tenderness in the left lower quadrant. There was no mass, muscle spasm, rigidity or free fluid. The glands in the groin were not palpable. Pelvic examination revealed a profuse purulent discharge issuing from the cervix. The cervix itself was red and inflamed. Bartholin's and Skene's glands were normal. The uterus was normal in size, position and consistency, but its mobility was limited and painful.

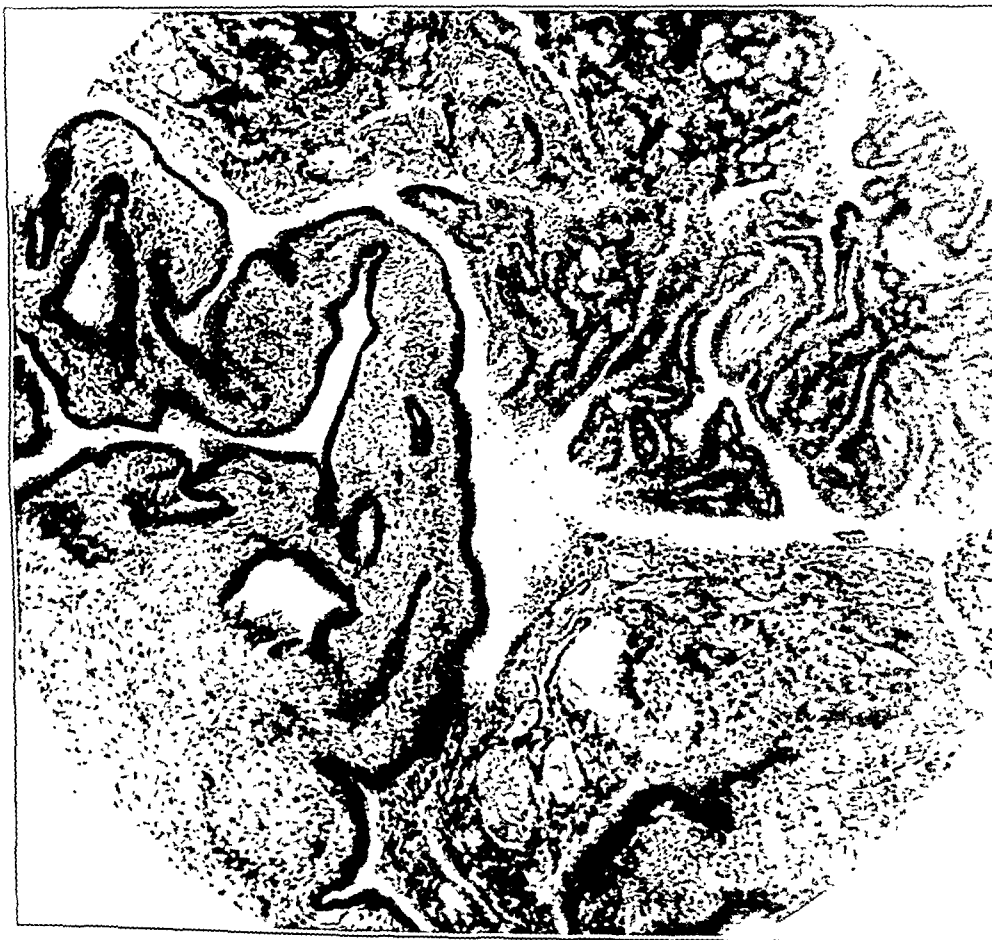


Fig. 5 (no. 31798).—Section through left tube showing three structures: (1) normal tubal papilla (left), malignant papilla (upper right) and solid carcinoma (lower right).

The adnexae were enlarged, adherent and sensitive. In the left fornix, there was a mass about 6 or 8 cm. in diameter.

Smears of the cervix showed that the pus contained some gram-negative diplococci. The catheterized urine was clear.

Treatment and Course.—The preoperative diagnosis was chronic salpingitis and cervicitis, probably gonorrheal in origin. In view of the chronicity and course of the disease, we advised that the patient be treated surgically.

One month later (in November, 1926), the operation was performed at the Hospital for Women of Maryland. The cervix was first thoroughly cauterized. The abdominal operation was performed through a midline suprapubic incision.

The omentum was so densely adherent to the anterior abdominal wall that the peritoneum had to be opened just below the umbilicus. The pelvic organs were completely covered by the thick, heavy omentum. The sigmoid was densely adherent over the left adnexae, which could not be seen but could be felt deep in the pelvis. The right adnexae were also adherent. The uterus contained a small fibroid tumor about as large as a marble.

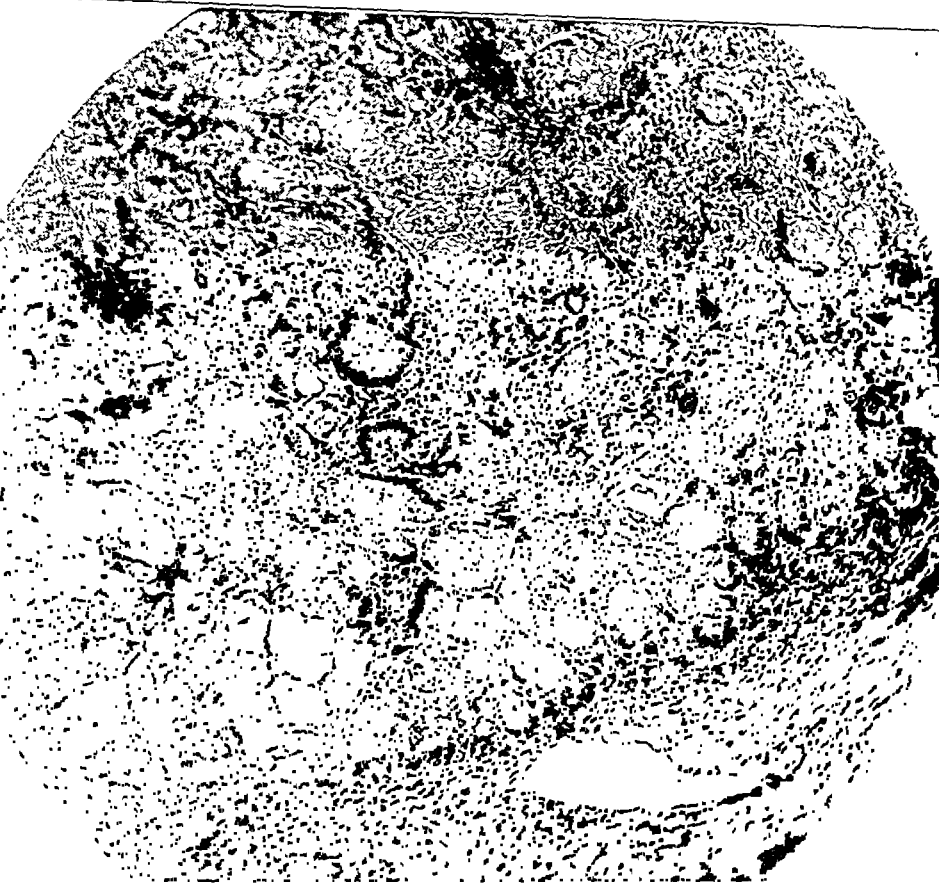


Fig. 6 (no. 31798).—Left tube showing alveolar carcinoma with marked lymphocytic infiltration and no invasion of tube wall.

The right ovary was riddled by small cysts; the right tube was closed. The left tube had the appearance of a fairly large hydrosalpinx, and under it one could feel the ovary, both fixed to the uterus and pelvic floor. While the left tube was being liberated, it ruptured, and a small papillary growth about 3 or 4 mm. in diameter popped out of it. It was firm, friable and grayish-white. With it escaped about 30 cc. of dark, serosanguineous fluid. We immediately gained the impression that

we were dealing with a carcinoma of the left ovary and decided to remove both tubes, ovaries and the supravaginal portion of the uterus. This was promptly done without accident.

There were no abdominal metastases or free fluid, and the pelvic glands were not enlarged. The convalescence was uneventful.

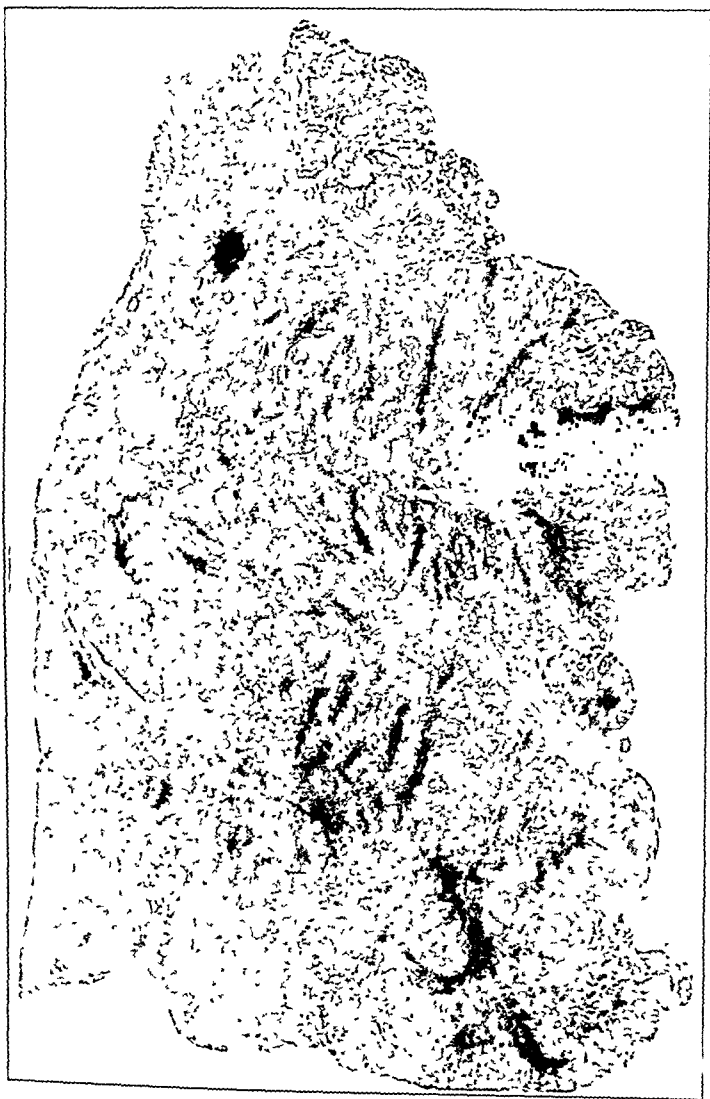


Fig. 7 (no 31798)—Carcinomatous tumor nodule expressed from lumen of left tube during operative manipulation. It was attached by a slender pedicle, $\times 8$.

We have seen this patient at intervals of about two months since the operation, and she has remained in perfect health, has gained in weight and has no discomfort. For a year after the operation, however, there was a good deal of pelvic induration which caused us some concern. Since it gradually was absorbed, we

decided that it was not a local recurrence, although we expected one. We sent the patient to Dr. Howard A. Kelly's sanatorium for radium treatment, but this was not given because of the continual improvement in the general health and the steady diminution in the pelvic induration. At the time this paper was written, more than two years after the operation, the patient enjoyed perfect health.

Gross Pathologic Examination.—The tissue included the supracervical portion of the uterus, both tubes and both ovaries. The uterus contained a small myoma,

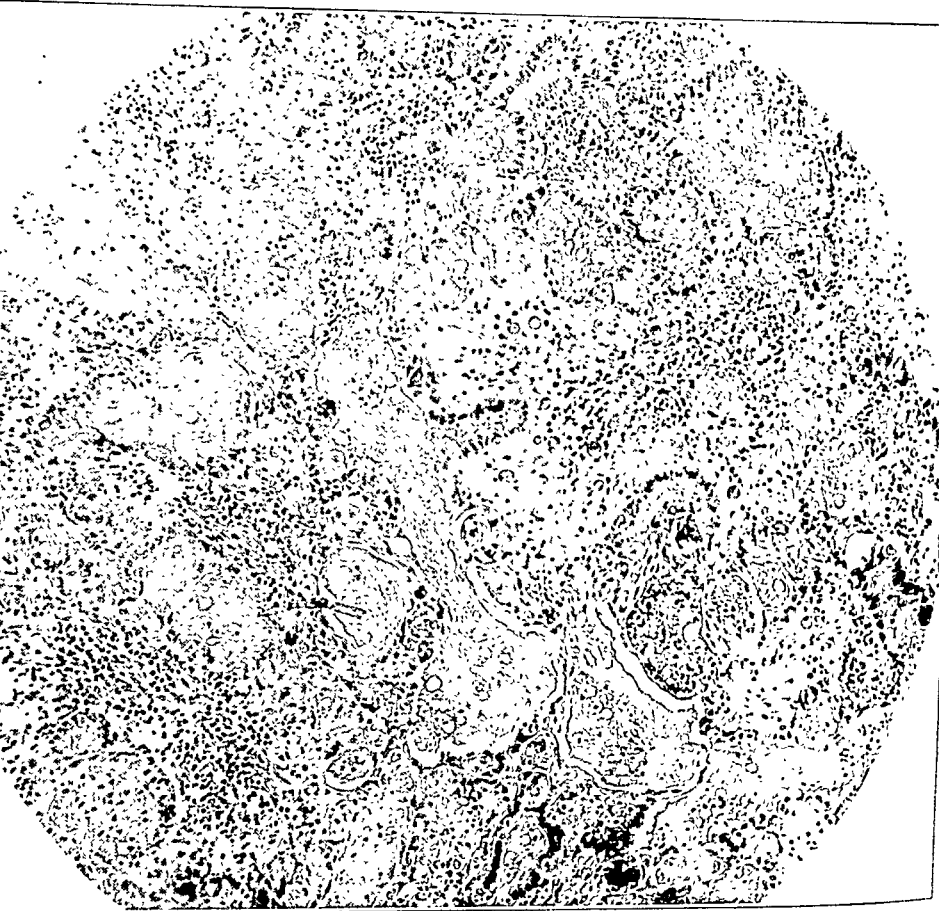


Fig. 8 (no. 31798).—Higher power view of tumor nodule shown in fig. 7, showing the alveolar carcinoma, delicate stroma, poorly differentiated papillae, and occasional mitotic figure.

about 2 cm. in diameter. The peritoneal surfaces were smooth, except for the raw areas caused by the adhesions and surgical dissection. No superficial metastases were evident.

The left tube was shaped like a retort; it had been opened, but still contained dark brown sanguineous fluid; numerous bits of tumor tissue flowed from the tube when it was opened further. The distal portion of the tube was hard and felt

solid. The fimbriated extremity was closed. The left ovary lay underneath and was adherent to the tube. The fimbriated extremity of the right tube was also closed. The right ovary was cystic and adherent to the right tube.

The uterine muscle was normal. The endometrium everywhere was smooth and pale.

Microscopic Pathologic Examination.—Left tube and ovary: Sections through the mass in the left tube showed that the tubal lumen was filled with a papillary growth, which was entirely limited to the tube and at no point had invaded the muscular wall. The mesosalpinx and ovary were normal. Under higher magnifi-



Fig. 9 (no. 31798).—Papilloma in right tube, which is frankly benign. Compare with fig. 5, which shows a malignant papilloma in the left tube.

cation, the tubal growth presented various pictures. The large papillary mass was frankly malignant, solid nests of carcinoma cells which presented marked variation in the size of the cells and nuclei being present. In general, the growth presented papillary and alveolar characteristics throughout. The tissue was studded with leukocytes and lymphocytes (figs. 6 and 8). The arrangement of the alveoli, the character of the cells, the variation in the size of the nuclei, their staining characteristics and mitotic figures stamped this growth as outspokenly malignant.

In other areas, the papillary tumors showed every gradation from the frankly malignant picture previously described to epithelial and glandular hyperplasia with little cytologic evidence of malignant disease. Some of these epithelial tufts varied from normal tubal papillae only in their greater size and the dense pattern of the growth. In the normal papilla the core of connective tissue formed the bulk of the tuft; in these hyperplastic growths, the connective tissue was scant and the epithelium dense, crowding out the stroma and destroying all resemblance to the simple structure from which it originated (fig. 5). In some of these tufts,



Fig. 10 (no. 29690).—The papillary type of growth, without invasion of the tubal wall, should be noted. Fimbriated extremity open. Recurrence and death in two months.

there were no mitotic figures, no significant variations in the size or staining characteristics of the nuclei and little heaping up of the epithelium. As in the case of adenocarcinoma of the body of the uterus, however, the pattern of the growth stamped it as a malignant process. In the same field, as in figure 5, one can find these adenomatous tufts, normal tubal papillae and outspoken islands of cancer side by side.

The right tube showed no active inflammation, the only evidence of salpingitis being the gross picture, the closed fimbriated extremity and adhesions. The

Summary of Fourteen Cases of Primary Tubal Carcinoma

Case No.	Age	Prim. Stage	Miscar. Stage	Symptoms	Inoperative Diagnosis	Operative Observations and Diagnosis	Operation	End-Result
1600	48	1	0	Menorrhagia; abdominal tumor	Myoma	Large uterine myoma; suspected tubal carcinoma not	Hysterectomy; bilateral salpingo-oophorectomy	Died in 5 months; peritoneal recurrence
2776*	63	1	0	Bloody vaginal discharge; fever 8 months	Pyosalpinx	Tubal mass like pyosalpinx; carcinoma not suspected	Hysterectomy; bilateral salpingo-oophorectomy; 1888	Recurrence in 1900; operation; well, 1902
2919	51	1	0	Pain in left side; watery, bloody, vaginal discharge	Retrosflexed uterus; salpingitis	Tube freely movable; vascular; few adhesions	(1) Left salpingo-oophorectomy; (2) curettage, two weeks later	Died, recurrence, 4 years
7071	58	1	0	Abdominal tumor; dyspnea	Large ovarian cyst	Ovarian cyst; tubal cancer not suspected	Left salpingo-oophorectomy	Lived 5 years; cause of death not known
9111	55	3	0	Bloody vaginal discharge; pain on defecation; pelvic pain	Myoma	Metastases in omentum; extension to rectum	Pan-hysterectomy; bilateral salpingo-oophorectomy; resection of rectum	Died, 6 months
11736†	46	0	1	Bloody vaginal discharge; abdominal mass; pain; leukorrhea	Pyosalpinx	Small uterus; enormous bilateral tubal cancer (figs. 2 and 3)	Hysterectomy; bilateral salpingo-oophorectomy	Recurrence in 3½ years
18153	47	0	0	Loss of weight; weakness	?	Ovarian cancer; appendix bound in tubo-ovarian mass; removed in toto	Appendectomy; right salpingo-oophorectomy	Recurrence and death in 13 months
18789‡	44	7	0	Abdominal pain; leukorrhea; dysuria	Myomata uteri; chronic salpingitis	Omental metastases; small myoma; chronic salpingitis	Hysterectomy; double salpingo-oophorectomy	Died 6 months later
19037†	47	0	0	Abdominal swelling; vomiting	Myoma; ovarian cancer	Clear fluid; peritoneal metastases; tubes open	Left salpingectomy	Died, 1 year
20090	46	0	0	Abdominal pain	Chronic salpingitis	Hydrosalpinx, left; degenerating mass in right tube, tensely adherent	Pan-hysterectomy; bilateral salpingo-oophorectomy	Died, 7 days; hemorrhage
31089†	43	3	12	Abdominal enlargement; pain	Pelvic tumor?	Carcinoma of pelvis, source undetermined	Partial removal	Died, 2 months
31798	29	0	0	Bloody vaginal discharge; abdominal tumor	Chronic salpingitis; cancer?	Chronic salpingitis	(1) Curettage, 1925; (2) curettage, hysterectomy; bilateral salpingo-oophorectomy, 1923	Well, 1 year
31798	29	0	0	Pelvic pain; leukorrhea	Chronic salpingitis	Small mass in tube; metastasis in endometrium	Hysterectomy; double salpingo-oophorectomy, 1923	Well, 1929
31111	52	0	0	Bloody vaginal discharge	Cancer of body of uterus		Curettage; hysterectomy; left salpingectomy, 1923	Well, 1929

* Reported by Hurdon (footnote 1).
† Reported by Vest (footnote 2).
‡ Reported by Cullen (footnote 3).

epithelium was normal almost everywhere. In one area, a definite papillary growth about 3 mm. in diameter (fig. 9) was found. It showed the same hyperplastic characteristics as similar growths in the left tube (fig. 10). There was a definite tendency toward heaping up of the epithelium; the alveolar pattern was dense, the connective tissue scant and compressed by the epithelial overgrowth. The individual cells showed no evidence of malignant disease, but the pattern was abnormal. In view of the condition found in the opposite tube, this adenomatous hyperplasia becomes particularly significant and forces us to the conclusion that it may represent the first step of the malignant process which was fully developed in the other fallopian tube.

Except for small graafian follicle cysts, the right ovary was normal. The myometrium and endometrium of the uterus were everywhere normal. The myoma showed no unusual characteristics.

Pathologic Diagnosis.—A diagnosis was made of primary carcinoma of the left tube; epithelial hyperplasia of the right tube; normal ovaries and normal endometrium; myoma of the uterus; chronic salpingitis.

SUMMARY

Primary carcinoma of the fallopian tube is one of the rarest of gynecologic diseases. It presents the usual incidence in regard to age. There seem to be no definite predisposing factors. The earliest and most constant symptoms are sharp, lancinating pelvic pain, associated with vaginal discharge which may at times be blood-tinged. Menstrual disturbances occasionally occur. The physical manifestations are variable. The diagnosis is extremely difficult, having been suspected in only one of more than 200 cases before operation. The treatment should be early removal of the uterus and of both tubes and both ovaries. The results of past treatment have been highly unsatisfactory. It is to be hoped that the results will be improved by earlier intervention and more complete extirpation. The malignant nature of the disease can usually be readily determined on the operating table by the routine macroscopic examination of tissues immediately after their removal.

LEUKOPLAKIA OF THE RENAL PELVIS*

ADOLPH A. KUTZMANN, M.D.

LOS ANGELES

Leukoplakia of the renal pelvis has been of increasing interest as indicated by its recognition in recent years. It is of interest to the pathologist because of its unknown pathogenesis and of clinical importance to the urologist for the diagnostic and therapeutic difficulties. It is a paradox, simulating an epithelial process (ectoderm) and yet occurring on the mucous membranes of the urinary tract, a structure of mesodermal and entodermal origin. The unsatisfactory treatment for leukoplakia, as well as the possibility of malignant degeneration, makes the condition one of clinical importance.

Leukoplakia of the renal pelvis occurs more frequently than is thought. Its infrequent occurrence is more apparent than real, the condition being overlooked through a laxity in observation of genito-urinary disease. Up to the present, sixty-seven proved cases have been recorded, inclusive of the case herein reported. Of the sixty-seven cases, forty-two were recorded prior to 1923, and twenty-five cases since, indicating that the condition is being recognized more frequently by all observers. While the observations are chiefly European, leukoplakia of the urinary tract has been increasingly recognized in recent years by American observers. Rokitsansky, in 1861, first mentioned leukoplakia in the bladder, and Ebstein, in 1882, described the first case of leukoplakia in the kidney. Cabot, in 1891, and Beer, in 1914, observed the first cases in the bladder and kidney, respectively, on this continent.

Because of the unknown etiology, important in the diagnosis, treatment and association with a malignant condition, it is essential to collect additional data and to stimulate an increasing recognition of leukoplakia of the renal pelvis.

REPORT OF A CASE

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History.—A Mexican housewife, aged 26, was referred by Dr. L. C. Audrain with the complaint of marked frequency of and burning on urination, soreness across the lower part of the abdomen and pain in the left lumbar region. The family history was irrelevant. The patient gave a history of measles, chickenpox and smallpox. She said that she had never had any venereal disease. The menstrual history was normal. There had been seven full-term pregnancies, with no miscarriages. The habits of the patient were good.

The condition began with pain in the left lumbar region and frequency of urination three years before Dr. Audrain saw the patient. Four months before, the patient developed tenderness across the lower part of the abdomen, with burn-

* Submitted for publication, May 24, 1929.

ing on urination and malaise. At the time of examination, she had marked frequency of urination, bordering on incontinence. The pains in the left lumbar region and lower part of the abdomen had increased in intensity. There seemed to be a sense of difficult urination with severe attacks of burning and occasionally a slight hematuria. There had been a marked loss in weight, but the patient did not know how much.

The physical examination showed an emaciated, sick-appearing woman, lying in bed and apparently in distress. The temperature was 99 F., the pulse rate 84, the respiratory rate 22 and the weight 97 pounds (44 Kg.). There was marked tenderness in the left lumbar region; this extended anteriorly and downward. The remainder of the physical examination was negative.

Examination of the blood showed hemoglobin, 65 per cent; red blood cells, 3,810,000; white blood cells, 11,400; polymorphonuclears, 74 per cent; small lymphocytes, 18 per cent; large lymphocytes, 4 per cent and large mononuclears, 2 per cent. Examination of the urine showed: extreme cloudiness; specific gravity, 1.018; light straw color; pH , 7.2; a heavy trace of albumin and no sugar. Microscopic examination disclosed numerous pus and red blood cells, and few epithelial cells. There were no casts. Phenolsulphonphthalein injected intramuscularly appeared in the urine as follows: 50 per cent in the first hour and 15 per cent in the second hour, a total of 65 per cent. The Wassermann reaction of the blood was negative.

On cystoscopic examination, the wall of the bladder showed a severe and diffuse cystitis; the capacity of the bladder was 30 cc. The vesical neck had a marked bullous edema. The right ureteral orifice was normal; there was marked ulceration around the left orifice. Both ureters were easily catheterized to the kidneys. The urine from the right kidney contained numerous red blood cells and an occasional white blood cell; there were no epithelial cells, no casts and no organisms. The urine of the left kidney was cloudy and tinged with blood. Microscopic study revealed numerous blood and pus cells and gram-positive cocci. The urine of the bladder showed a similar picture. No tubercle bacilli were found in any of the specimens. All cultures failed to grow although staphylococci were the predominating organisms in the stained smears. Phenolsulphonphthalein, injected intravenously, appeared in three and one half minutes on the right side and returned 32 per cent of the dye in thirty minutes. The time of appearance in the left kidney was five minutes, with 14 per cent secreted in thirty minutes. There was no leakage from the bladder. Pyelographic studies showed a left pyonephrosis (fig. 1).

The diagnosis was left pyonephrosis with cystitis and a contracted bladder.

Because of the patient's marked anemia, a blood transfusion was given two days before the operation. A left nephrectomy was performed under ethylene oxygen anesthesia. Convalescence was uneventful except for an infection of the wound, which cleared up readily under daily irrigations with surgical solution of chlorinated soda (Dakin's solution).

When the patient was seen, six months later (Dec. 1, 1927), she had gained 20 pounds (9 Kg.) in weight, felt well and was able to do her housework. Nocturia occurred twice and diuria every two or three hours. The remaining signs and symptoms had cleared up entirely. She did not return for further observation of the bladder.

The specimen consisted of a left kidney weighing 190 Gm. The surface was very rough, a mottled purplish pink, and irregular. On section six irregular cavities were seen which were connected with each other and with the pelvis. The pelvis and cavity-like calices were covered by a whitish, wrinkled, thick, parch-

ment-like membrane (fig. 2). The remainder of the renal parenchyma showed little differentiation and was swollen in appearance. The capsule stripped with difficulty; a coarsely scarred surface remained.

Microscopic Examination.—Many areas of the kidney had been replaced by inflammatory products composed of small round cells, eosinophils and some leukocytes and connective tissue, in certain areas approximating abscess formation. The adjacent tissue of the kidney showed edema and cloudy swelling. The tubules appeared to be slightly dilated, as did some of the glomeruli, while others were sclerosed and congested. The blood vessels showed marked fibrosis. Everywhere the interstitial connective tissue was increased (fig. 5).



Fig. 1.—Left pyelogram (20 per cent colloidal silver iodide compound), showing the picture of a typical pyonephrosis.

Examination of the pelvic mucosa showed a definite metamorphosis into squamous epithelium similar to the skin. There was a marked chronic inflammatory reaction, chiefly of small round cells, beneath this process and in some areas infiltrating it. The squamous epithelium showed a cornified layer beneath which was a granular layer of cells (keratohyaline granules). Underneath could be seen a well defined basal layer. Some sections showed a tendency toward papillary downgrowth of this layer. The entire picture was that of a well defined leukoplakia (figs. 3 and 4).

The final diagnosis was chronic pyonephrosis with pelvic leukoplakia.

COMMENT

This case definitely demonstrated a leukoplakia which appeared to be limited to the renal pelvis and calices. It was associated with or complicated by an infection of long duration, a severe pyonephrosis which had practically destroyed the kidney. In all respects, this case definitely simulated the various cases of leukoplakia reported in the literature. In accord with the present theories of leukoplakial pathogenesis, it may be considered as associated with or due to the severe chronic infection of the urinary tract.



Fig. 2.—Sagittally sectioned kidney of reported case, showing the white skin-like areas covering most of the pelvis and calices and extending in patchlike formation to the ureteropelvic junction. The pelvic wall and ureter show marked thickening. The calices present the picture of a pyonephrosis.

PATHOLOGIC ANATOMY

The occurrence of cornified squamous epithelium on the mucous membranes of the body has always engrossed the interest of observers. Distributed throughout the various parts of the body, it has been named leukoplakia, metaplasia, prosoplasia, epithelismetaplasia, pachydermia, xerosis, cholesteatoma, leukoplasia, psoriasis membranacea

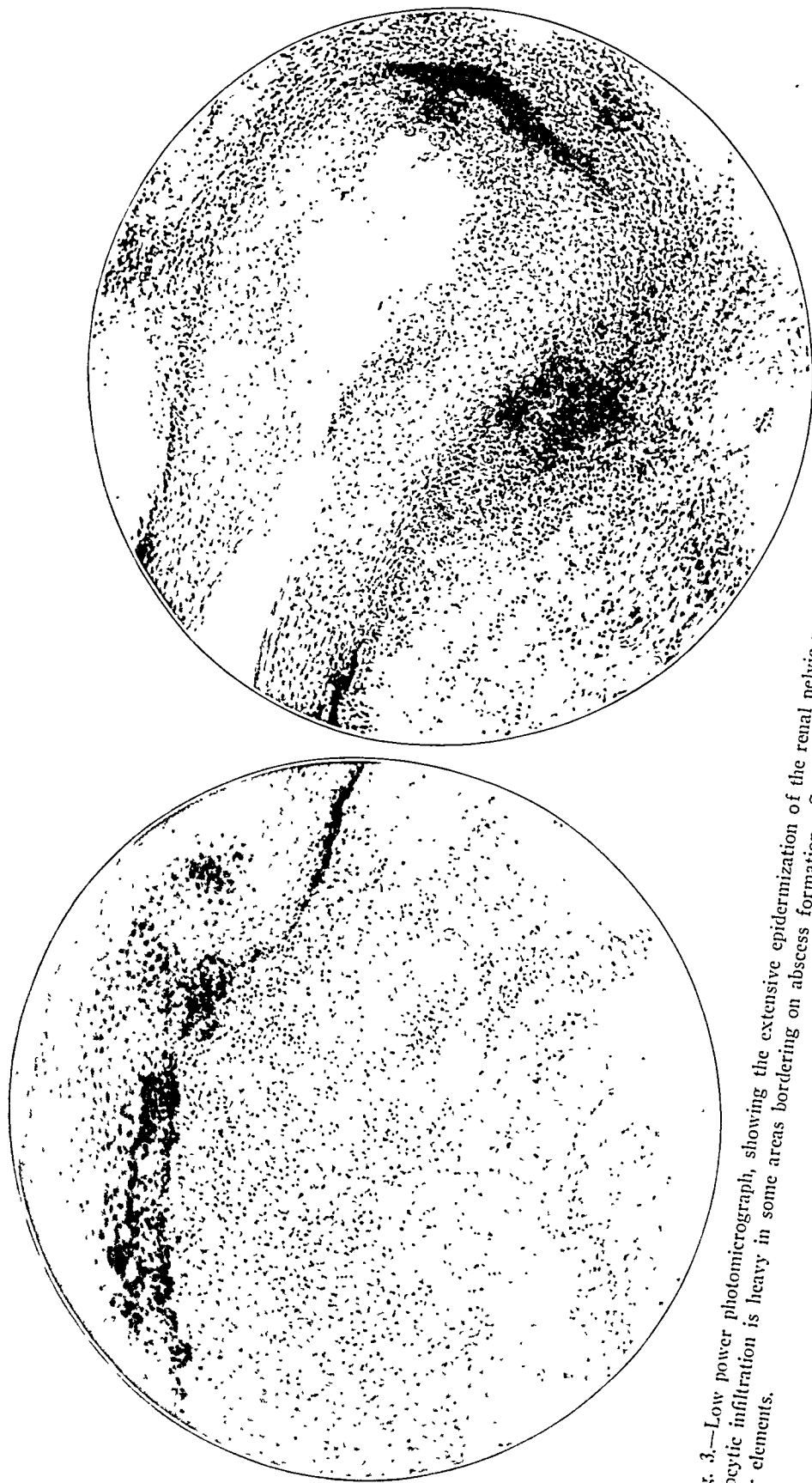


Fig. 3.—Low power photomicrograph, showing the extensive epidermization of the renal pelvic mucous membrane. Note the marked resemblance to skin. The lymphocytic infiltration is heavy in some areas bordering on abscess formation. Some parts of the leukoplakic membrane show infiltration with inflammatory cellular elements.

mucosae, leukokeratosis, tylosis and epidermal plaques. It has been found on the mucous membranes of the tongue, mouth, gums, esophagus, gallbladder, rectum, nose, frontal sinuses, ear-drums, vagina, uterus and the urinary tract.

The morphology of leukoplakia is described uniformly by nearly all observers. As the term signifies, leukoplakia refers to the formation of white patches on mucous membranes, although it may also include

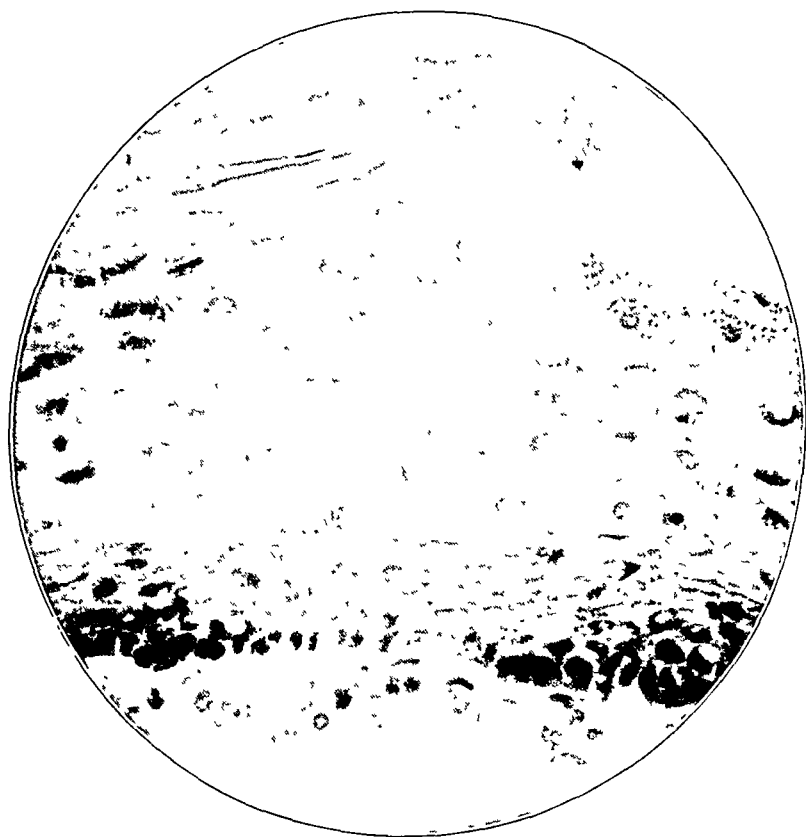


Fig. 4.—High power photomicrograph, showing the epidermization process of the pelvic mucosa with the keratohyaline granulation of the stratum granulosum well defined beneath the lamellated desquamating layer.

those forms found on the surface of the skin and described as a xeroderma or keratosis. Pathologically defined, it consists essentially of a thickening or keratinization of epithelium taking on a definite epidermoid character, regardless of location in the body. In the pelvis of the kidney there can be found well defined skinlike membranes, whitish or grayish, pearly or silvery, with a surface in fine or coarse

folds. Usually the pelvis is covered with areas ranging from a very small to a large size and in some instances lining the entire pelvis. This leukoplakial membrane is dense and resistant and often can be dislodged with difficulty. The denuded underlying tissues will then show a papillary surface.

Microscopically, the leukoplakial membranes bear a definite resemblance to skin, presenting the characteristic layers of the stratum



Fig. 5.—Destruction of the renal parenchyma. Note the marked increase of fibrous tissue interstitially, and the vascular sclerosis; the damaged glomeruli and marked lymphocytic infiltration border on abscess formation.

germinatum, mucosum, granulosum lucidum and corneum. The granular layer shows the typical keratohyaline granules seen in the skin, and the cells of the rete show the typical intercellular bridges. A marked lymphocytic infiltration of the underlying connective tissues due to the accompanying inflammatory conditions is present.

Some observers have attempted to differentiate two types of epithelium. The first type mentioned by Lavonius, Ikeda, Hallé and

Englisch is similar to the epidermis. There is seen a single row of cylindric basal cells topped by the prickle cell layer, with the keratohyaline granular layer next and the cornified layer on top. The epithelium differs, however, from the true epidermis in that the structure is irregular and the thickness of the layers is variable, as mentioned by Englisch. Furthermore, Hallé has shown that the epithelium of leukoplakia possesses a stronger power of growth which manifests itself in a double tendency, on the one side to a proliferation of the deep layers noted by Francke in his cases and thought by Englisch to be rare, and on the other, to a marked desquamation of the upper cornified layer. This might result in a filling of the urinary tract with cholesteatomatous material. According to Karo, leukoplakia and cholesteatoma are not the same, their origin only being common, with leukoplakia as the primary disease. The latter leads to the shedding of wide, cornified, epithelial fragments which may collect into a tumor-like, pearly, onion peel-like, stratified epithelial mass, generally termed "cholesteatoma," and later cause an obstruction in the urinary tract. "Cholesteatoma," according to Corsdress, is a misleading term since there is no true formation of tumor in a pathologic sense. According to the researches of Schridde, it is designated as early leukoplakia, without cornification, as differentiated from true leukoplakia, which is characterized by a true cornification of the epithelium.

A still further differentiation from epidermis is that the cornification is not completely developed. The cornified layer stains with the Gram as with the Gram-Weigert stain (Ernest), while it will not retain the golden orange when tested according to the method of Ebbringhaus. Lavonius observed in this type still another difference in that a layer of flattened cells without granules and nuclei lies above the lamellated layer.

In the second type, over the lowermost layer of prickle-cells there lie several rows of polygonal, less flattened cells with round or comma-shaped nuclei and with a lightly-staining protoplasm. The cornified and eleiden layers are frequently missing. There are present only a few cells of the keratohyaline layer. This type corresponds to the so-called third type of Hallé and to the second type of Ikeda and Lavonius. The second type of Hallé and Englisch, in which the cornified layer lies on a few rows of basal cells, does not appear to be frequent.

The type of epithelium described by Stoerck and Lichtenstern in which the upper cell layers simulate nucleated scales, while the lower cells cannot be differentiated from the ordinary transitional epithelium, approaches a third type of Ikeda and simulates the beginning stage of the others, yet does not belong to leukoplakia. The epidermis-like character of the superficial layers, as well as the characteristic single

basal cell layer with several prickle-cell layers overlying, cannot be separated from the picture of leukoplakia.

Pathogenesis.—The occurrence of leukoplakia in the urinary tract presents a paradox in that one finds an ectodermal type of structure occurring in organs of mesodermal and entodermal origin. This has been the subject for many theories. The condition has been noted in many parts of the body, Virchow describing it as pachydermia laryngis and von Graefe as xerosis of the conjunctiva; Schönemann noted the occurrence of cornified squamous epithelium in ozena of the nose, while Zeller and R. Meyer found it in the uterus, and Deetz in the gallbladder. Rokitansky, in 1861, was the first to describe leukoplakia in the urinary tract when he noted that "in the inflamed bladder there occurs occasionally an epidermoid production, at times circumscribed, at other times occupying the whole mucosa of the urinary apparatus; it produces an abundant desquamation of thick scales, stratified, white, shiny, in the form of cellular epidermoid plates; the adjacent mucosa is chronically inflamed and villous."

Various observers have sought to explain the leukoplakic process on the basis of some disease. Many years ago, Hunter and Babington, and later Schwimmer, noted that the epidermization of mucous membranes was not necessarily due to syphilis. Syphilis, while discarded, recently received support from S. and E. Li Virghi. Tuberculosis, found as an associated condition by some observers, has been accorded some consideration from Beselin and the Nordique-Lavonius school. Such theories as that of substitution, in which the epidermization was thought to extend into the urinary tract through some fistulous opening, has long been discarded. This was originally advanced by Eicholz, Posner and Marchand. Marchand later supported the theory of metaplasia.

The congenital theory and the theory of cell rests (*Keimversprengung*) have had many advocates. Lecène, in promulgating this theory, noted that there might be an arrest of development of the urinary tract by what he called an epidermoidal heteropia. The wolffian body, from which the ureter and pelvis are developed, shows a complex development, and since at some time there may be an intimate relationship with the ectoderm, ectodermal cells may be included. Studies on embryos have shown that during a certain time the excretory canal of the pronephros is included in the ectoderm. Staehlin, R. Meyer, Guinard and others stated that the pronephric portion of the wolffian body is of ectodermal origin and that the embryogeny of the urogenital system may be complicated by such misplaced cells from the primitive ectodermal layer and give rise to the growth of these aberrant cell rests subsequently found in the genito-urinary tract. It has been found that there may be pavement epithelium in the urinary tract.

Lavonius examined 150 renal pelves according to the method of Zilliakus, and microscopically demonstrated five cases in which leukoplakia might originate. A case was observed by Leber in a girl, aged 4 months, with xanthoma of both conjunctivae together with proliferation of the epithelium of the pelvis.

Not infrequently small areas occur in the urinary bladder in which the epithelium shows *cornification*. Lubarsch, in 160 autopsies, found six cases with islands of leukoplakia, while Heymann noted small circumscribed areas of cornification in ten of twenty cases. Ribbert and Albarran held that these islands of flattened epithelium were of embryonal origin and later underwent leukoplakial degeneration. Ribbert pointed out that these cells which may appear normal in this location nevertheless possessed embryonic potentialities and that some of these cells were partially differentiated and could undergo changes more readily; moreover, that the newly developed cells were not as highly specialized as the preexisting cells and that the leukoplakial change might occur only in the presence of certain abnormal conditions. Zeller, in his work, showed many cases with pavement epithelium in the uterus to which he attributed an etiologic rôle in the cause and continuation of endometritis. From the evidence submitted, the congenital theory and the theory of cell rests are not sufficient to explain the transformation of the cylindric epithelium into flat epithelium. The universal association with a long-standing infection is left unexplained, unless it were accepted that leukoplakia invited infection, but clinical data hardly substantiate this theory.

The theory of metaplasia, supported by many authors, has lent itself best to the explanation of most cases. The idea of metaplasia which originally had a loose meaning has in the course of time assumed a more specific aspect. At present, only a process in which the new epithelium does not develop from the original anlage is designated as a metaplasia of the epithelium. In some cases in which cornified squamous epithelium is found on a mucous membrane where transitional epithelium originally is normal, it has been conceived that there might have been an abnormally continued development of the transitional epithelium, termed by Schridde as "*prosoplasia*." This was also known as an "*indirect metaplasia*" in contrast to Virchow's view in which he defined metaplasia as a "*direct change of one cell into another cell which was architecturally different but had not completely given up its characteristic structure*." In the light of present knowledge of metaplasia, Orth has more accurately defined it as the transformation of a well characterized tissue into another tissue that is equally well defined but morphologically and functionally different.

Haythorn especially dwelt on metaplasia in accounting for the epidermoid changes in the bronchi. His studies as well as those in

recent years by Francke, Allemann, Karo, and Hinman and Gibson have been increasingly supported by observers until now it is the most widely accepted theory. Haythorn's theory in reality supports the older views of Schridde so far as he considers the metaplastic cells as newly formed cells and that they come from the growing layer. Ribbert's view also is supported in that the newly formed cells are less highly specialized than the normal cells, and that the changes in the surrounding tissue have a strong influence on the type of new cells formed. Since all cases are associated with long-standing chronic infection, it is thought that the mucosa is destroyed by a progressive process. The damage may be profound and exhausting and may include the basement membrane. Being unable to regenerate their own type, the cells bring forth a more protective cornified type. The mucosa in its exhausted condition and beyond specific regeneration seeks to protect itself with the best type of reparative cell it can produce. There is also probably a link between the injury to the basement membrane and tumor growth, and hence the irritants and inflammation which destroy them open the way for metaplasia and new growth. The process involving the basement membrane therefore favors metaplasia. By this type of hyperplasia, the loss is covered and a new cell with apparently increased resistance appears. This active defense is assumed to occur in the comparatively mild infections and irritations acting over a longer period; if the irritating factors are more intense, an excessive hyperplasia may occur, breaking through the borders and developing into a malignant condition. The desquamated cells have been found to contain glycogen. Even the most rudimentary types of metaplasia contain it, and it is entirely lacking in the normal epithelium (Schiele, Gierke and Ikeda).

Küttner and Klug considered leukoplakia on the basis of tumor formation. Corsdress differed from this opinion, considering cholesteatoma as not being a real tumor since there is no multiplication of cellular substance characteristic of tumors, but only a transformation of the character of the cells.

Leukoplakia has been considered as an irritative lesion, on the basis of bacterial toxins, similar to malakoplakia, cystitis cystica, trigonitis granulosa, polyposis of the vesical neck and venereal condylomas. Briggs and Maxwell, and Kretschmer analyzed the bacteriology of collected cases, but were unable to reach any conclusion. Leber believed that there must be some specific bacterial irritant to cause the cornification, since he found the same type of bacteria on the leukoplakia of the renal pelvis as on the xerosis of the conjunctiva. In support of this fact, Kuschbert and Neisser designated a xerobacillus as the cause, although its harmlessness was later demonstrated by

Schreiber and Neisser. It is possible for leukoplakia to occur without the presence of microbial infection, as was demonstrated by Escat in his cases of tumors of the bladder on a leukoplakic basis.

Many questions still remain to be solved. While it is assumed by most observers that leukoplakia is caused by a chronic irritation, whether inflammatory, chemical or mechanical, why are there so comparatively few cases of leukoplakia in comparison to the numerous cases of pyonephrosis, hydronephrosis or nephrolithiasis? Granting the process to be a metaplastic one in epithelial changes, why does a leukoplakia occur on one occasion and pyelitis cystica on another? When the leukoplakia has become a fully developed process, why are there well defined areas of it, while the adjacent epithelium exposed to the same pathologic influences remains unchanged? Finally, since there is a cornification which has been explained by Recktenwald, Hinman and others as a protective measure against destructive irritation, why should such a process proceed to a more pathologic condition such as carcinoma?

Relation to Malignant Disease.—The evidence is slowly increasing that leukoplakia may be the forerunner of the squamous cell carcinoma (Hinman and Gibson, Scholl, Kretschmer, von Borza and Patch). An analysis of the sixty-seven collected cases of leukoplakia of the kidney has revealed seven squamous cell carcinomas and one adenocarcinoma, an incidence of 11.9 per cent. Of these, six occurred in the renal pelvis (Kischensky, Spiess, Aschner, Thomson-Walker, Patch and Fuetterer [adenocarcinoma]) and two in the bladder (Rona and Recktenwald). Patch, in a recent review of the literature, found 152 cases of squamous cell carcinoma in the urinary tract—36 renal, 6 ureteral and 110 vesical cases—showing that this type of malignant disease is not rare. A further analysis revealed thirteen cases in the kidney and bladder which had leukoplakia and squamous cell carcinoma coexisting. These figures show a greater occurrence of these conditions than is surmised by many observers. Added significance should therefore be given to Hinman and Gibson's theory that leukoplakia is the forerunner of the squamous cell carcinoma. Leukoplakia, while being a physiologico-metaplastic process, may therefore become a pathologic one in some cases. Its presence alone would tend to maintain an incurable state of chronic inflammation and irritation. The latter maintain a continuous activity of epithelial proliferation as a protective process. Should this proliferative activity and destruction continue over a period of time, these cells may then show a malignant change. Just why a defensive process such as leukoplakia could be stimulated to undergo a malignant change is one of the weaknesses of this theory. Yet the evidence submitted from time to time is becoming more supportive. Patch recently demonstrated the transitional

stages in a case in which repeated examinations disclosed lesions of an intermediary type which, while not definitely malignant, were undoubtedly precancerous. Hinman, Kutzmann and Gibson demonstrated in one of their cases, although not so definitely, an early papillary downgrowth with a beginning break in the basement membrane suggestive of malignant disease, and therefore considered it as precancerous. Kretschmer has referred to leukoplakia, stone and chronic infection as the recognized forerunners of nonpapillary carcinoma of the renal pelvis.

Von Borza, in describing squamous cell carcinoma, considered not only local but also constitutional factors, such as the endocrine system. The hormones, being distributed as chemical irritants through the body.

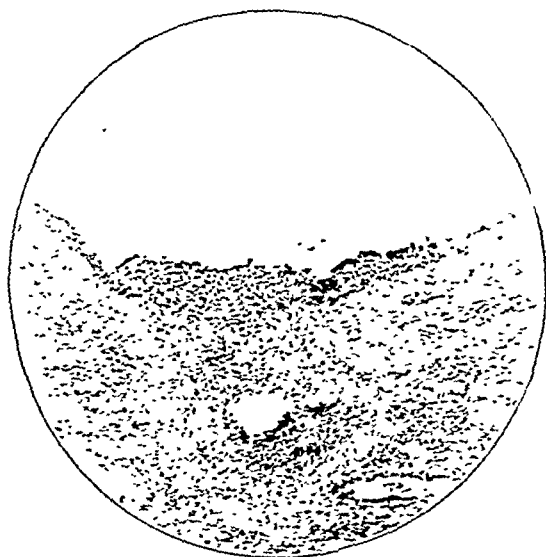


Fig. 6.—An incipient stage of squamous cell metaplasia (leukoplakia) on the mucous membrane of a renal pelvis. There can be seen the normal transitional epithelium at the left, and the denuded epithelium and basement membrane on the right. Beneath these is a thick layer of granulation tissue infiltrated with lymphocytes. (Courtesy of Dr. Frank Hinman.)

have a specific action on the cells and tissues. He cited Biedl and Hertwig who stated that every organ, tissue and cell can be changed in its relationship by a change of one specific hormone to another. The toxins of the rapidly increasing cells lower the resistance and there is nothing to hinder local growth.

Wolbach, in conjunction with Howe, made some interesting pathologic observations in the deficiency diseases or the avitaminoses. In vitamin A deficiency, known as xerophthalmia or keratomalacia, a striking and extensively distributed epithelial metaplasia was found in

the conjunctivae, ocular glands, alimentary tract, respiratory tract and genito-urinary tract. It was noted that the epithelium was replaced by stratified keratinizing epithelium, strongly resembling leukoplakia. Wolbach found that a number of the experimental animals (rats) with this disease died of obstruction in the genito-urinary tract caused by its occlusion with desquamated keratinized epithelial cells.

Clinical Picture.—Symptomatically, leukoplakia of the renal pelvis per se presents nothing singular or characteristic. The outstanding points are the associated urinary infectious diseases and their chronicity. The leukoplakia itself is not discovered until operation or at autopsy, treatment being instituted for the associated condition.

Leukoplakia of the renal pelvis occurs more frequently than is thought, but has probably been overlooked through lax observation of pathologic conditions of the genito-urinary tract. A review of the literature reveals sixty-seven cases inclusive of the case herein given. The rarity of the condition seems to be only apparent. Patch noted that up to 1929, 123 cases had been reported in the entire urinary tract exclusive of the urethra.

Leukoplakia may occur in any portion of the urinary tract from the renal pelvis to the urethra. Stevens, Blum, Czerny and Bugbee even reported cases of diverticulum of the bladder containing leukoplakia. Briggs and Maxwell analyzing eighty cases in the urinary tract, including those reported and their own, found the following distribution: vesical forty, renal twenty-four, renal and ureteral ten, ureteral and vesical four, and renal or ureteral or both two. Since the division is almost equal—forty-four vesical and forty renal cases—they concluded that it must occur more frequently in the kidney, this diagnosis being made only at operation or necropsy, while the vesical cases might be more often diagnosed by cystoscopic observation of the bladder. Sixteen of the collected sixty-seven kidney cases had leukoplakia elsewhere: seven in the ureter, four in the entire urinary tract, two in the bladder, two in the ureter and bladder and one in the eye.

Leukoplakia of the renal pelvis may occur at any time during life, its greatest frequency, however, being in the fourth decade, the third and fifth decades following. The youngest patient reported was 4 months (Leber) and the oldest 70 years of age (Hallé) (fig. 7).

Leukoplakia of the renal pelvis occurs equally in both sexes. In the sixty-seven collected cases it was found in twenty-nine males and twenty-eight females, ten cases not being stated. This observation confirms an earlier report of Hinman, Kutzmann and Gibson and is at variance with Hennessey in whose recent review of seventy-five cases of leukoplakia throughout the urinary tract, fifty-six were in the male and nineteen in the female, a ratio of 3:1. Corsdress also found leukoplakia of the urinary tract in general to be more prevalent in males

in the ratio of almost 2:1. The latter observations, however, seem to be true of leukoplakia in the lower part of the urinary tract.

The distribution of the leukoplakia in the sixty-seven cases as to sides was right thirty-two, left seventeen, bilateral three and not stated fifteen. From this it may be noted that the condition tends to be unilateral, which is of importance in the treatment.

While there are some reported cases of uncomplicated leukoplakia in the urinary tract (bladder) (Escat and Allemann), leukoplakia of the renal pelvis nearly always has an associated infection. Some authors have given the bacteriology especial mention; the type of organism probably is of small consequence, there being such a variation in bacteriologic data in the collected case reports. It is a fact that there

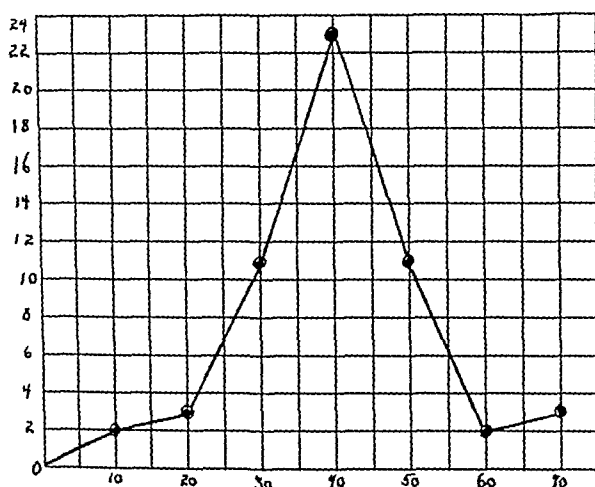


Fig. 7.—Curve, showing the age incidence in fifty-five collective cases of leukoplakia of the renal pelvis.

is an infection present which is of importance and has made most observers feel that it plays an important part in the pathogenesis. The frequent presence of cystitis, pyonephrosis, tuberculosis, lithiasis, etc., is to be noted. Table 1 shows an analysis of the sixty-seven collected cases which are distributed as follows: cystitis, forty-four; pyonephrosis, forty-one; stone, twenty-five; hydronephrosis, thirty-one; tuberculosis, ten; carcinoma, eight.

This analysis emphasizes the coexistence of infection and stone with the leukoplakia and points strongly toward the possibility of this process being an etiologic irritative factor. The finding of five squamous cell carcinomas (Kischensky, Spiess, Thomson-Walker, Aschner and Patch), one adenocarcinoma (Fuetterer) and two vesical squamous cell carcinomas (Rona and Recktenwald) are evidence supporting Hinman

TABLE 1.—*Conditions Associated with Leukoplakia of the Renal Pelvis*

Case	Author	Cystitis	Tuber- culosis	Hydrone- phrosis	Pyelo- nephritis Pyone- phrosis	Stone	Carci- noma	Leuko- plakia Elsewhere	Miscel- laneous
1	Allemann	+	+	General- ized	Uremia
2	Allemann	+
3	Allemann	+	+
4	Aschner	+	..	+	..	+	Squamous cell carci- noma in ureter	Bladder	Bilal pelvis
5	Beer	+	Orthostatic albuminuria
6	Beer	..	+
7	Beselin	+	+	+
8	Braatz	+	+	Interstitial nephritis
9	Biondi	+	+
10	Briggs and Maxwell	+	+	Addison's disease
11	Briggs and Maxwell	+	+
12	Busse	No data given
13	Chiari	+	+	+	..	Ureter and bladder	Both renal pelvis dilated Nephritis at age of 16 years
14	Chiaudano	+	+
15	Chiaudano	+	..	+
16	Corsdress	+	..	+	+
17	Crabtree	No associated pathologic condition of any type; hematuria the only sign present
18	Cummings	+	..	+	+	In bladder
19	Ebstein	+	+
20	Ebstein	+	+	Ureter	Cystic cystica Ureteral stricture and peri- urethritis Uremia
21	Francke	+	..	Bilateral	..	In bladder
22	Fulci	+	..	+
23	Fuetterer	+	Adeno- carcinoma
24	Hallé	+	+	..	Both ureters and bladder	..
25	Hallé	In bladder	..	Both pelvis, ureter and bladder	..
26	Hallé	+	+
27	Hinman	+	..	+	+	+
28	Hinman, Kutzmann and Gibson	+	..	+	+	Bladder	..
29	Hinman, Kutzmann and Gibson	+	..	+	+	Right neph- roptosis
30	Israel	+	..	+	+	+
31	Israel	+	Double kid- ney pelvis; uremia
32	Jura	+	..	In ureter
33	Karo	+	In ureter	..
34	Keane and Denis	+	..	+	+	In ureter	Ureteritis
35	Kischensky	+	..	+	+	..	Squamous cell carcinoma of pelvis	In ureter	..
36	Kraul	+	..	+	+
37	Kretschmer	+	+
38	Kretschmer	+	..	+
39	Kretschmer	+	+	..	+
40	Kretschmer	+	..	+	..	+	Ureteral stricture, also attacks of urethral calculi

TABLE 1—Conditions Associated with Leukoplakia of the Renal Pelvis—Continued

Case	Author	Cystitis	Tuber- culosis	Hydrone- phrosis	Pyelo- nephritis Pyone- phrosis	Stone	Carci- noma	Leuko- plakia Elsewhere	Miscel- laneous
41	Kretschmer	+		+				Ureter	Median bar at vesical neck
42	Klug			+		+			
43	Klug	+	+		+				
44	Kuettner	+		+	+	+			
45	Kutzmann	+			+				
46	Lavonius	+			+	+			
47	Lavonius		+		+			Ureter	
48	Lavonius	+			+			..	
49	Lavonius		+		+			..	
50	Lavonius		+	.	+			Eye	Congenital
51	Leber								..
52	Lecene	+		+	+			Generalized	Uremia; urethral fistula
53	Liebenow	+			+	+			No data given
54	Michon								Uremia; obstruction at vesical neck
55	Patch	+			+	Kidney, ureter and bladder	Squamous cell carci- noma of left kidney and bladder	Both kidneys and bladder	
56	Pedroso and Lequerica				+	+			
57	Pedroso and Lequerica			+	+				
58	Pollack								No data given
59	Rafin	-		+		+			
60	Recktenwald	+		+			Squamous cell carcinoma of bladder		
61	Richey	+		+	+				
62	Romiti	+		+	+	+			Foreign body in renal pelvis
63	Rona	+		+	+	Kidney and ureter		Left ureter	
64	Rona	+	+		+		Squamous cell carcinoma of bladder		Pulmonary and genito urinary tu- berculosis
65	Spieess				+	+	Squamous cell carcinoma of pelvis		
66	Stockmann	+			+				Right ureter dilated
67	Thomson- Walker	+		+	+	+	Squamous cell carcinoma of pelvis		
Total		44	10	31	41	25	8	16	

and Gibson's idea that leukoplakia is not altogether a physiologic but also a pathologic process. Miscellaneous associated conditions have been orthostatic albuminuria (Beer), interstitial nephritis (Braatz), cystitis cystica (Ebstein), double renal pelvis (Israel), infancy (Leber), foreign body in the renal pelvis (Romiti), calculus in the opposite kidney and ureter (Rona) and Addison's disease (Briggs and Maxwell)

Symptomatology—There are no pathognomonic symptoms of leukoplakia of the renal pelvis. Most cases present the signs and symptoms of the coexisting or associated condition, the usual one being a urinary infection of long duration. The true condition is almost never diagnosed except at operation or autopsy. An exception

TABLE 2.—*Leukoplakia of the Renal Pelvis*

Case	Author	Date	Age, Years	Sex	Side	Initial Symptoms	Duration	Anatomy
1	Allemann.....	1926	23	M	Left	Dull pain in region of kidney; hematuria	Leukoplakia of renal pelvis with suppurative nephritis
2	Allemann.....	1926	27	M	Right	Hematuria and cystitis	10 years	Typical leukoplakia of pelvis with areas of pus in parenchyma Complete epidermization from urethra up to both renal pelvis;
3	Allemann.....	1926	..	F	Bilateral	Acute and persistent cystitis	bilateral hydro-ureter and pyelonephritis with cortical abscesses;
4	Aschner.....	1922	38	M	Right	Attacks of stabbing pain in right flank	3 weeks	Lower pelvis and calices contain grayish-white, creamy flakes; mucosa almost covered by dull, grayish-white, elevated irregular membrane; squamous cell carcinoma at ureteropelvic junction; infected hydronephrosis; calculus
5	Beer.....	1914	20	M	Left	Orthostatic albuminuria; cystitis	3 years	Pearly white plaques in the urine
6	Beer.....	1914	35	M	Left	Pain in left flank, radiating to scrotum	9 months	Leukoplakia with lower half of the pelvis, about the size of a silver dollar, associated with tuberculosis
7	Beselin.....	1885	35	M	Right	Attacks of renal colic	17 years	Hydronephrosis; pelvis covered with white pearly membrane; also tuberculosis
8	Blondl.....	1904	Greater part of pelvis lined with a leukoplakia; pyelonephritis; hydronephrosis
9	Bratz.....	1898	33	F	Right	Attacks of renal colic	2 years (?)	pelvic mucous membrane had appearance of epidermis; interstitial nephritis
10	Briggs and Maxwell	1926	37	F	Left	Attacks of renal colic; cystitis	12 years	Pelvis lined with stratified squamous epithelium; pyelonephritis with pyelocystia; Addison's disease
11	Briggs and Maxwell	1926	37	F	Right	Renal pain on right side	15 years	Renal pelvis lined with typical stratified squamous epithelium, showing considerable cornification; pyelonephrosis
12	Busse.....	1904	..	F	Pyelitis and cystitis...	Parts of renal pelvis showed a leukoplakia; renal calculus
13	Chlari.....	1888	34	F	Hydronephrosis; mucous membrane thick and epidermoid; also renal calculus
14	Chiaudano.....	1924	37	M	Right	Nephritis at 16 years of age; occasional burning on urination	21 years	The lower two thirds of the pelvis and part of ureter showed a rough whitish, shiny and ulcerated, epidermis-like membrane; pyelonephritis with abscesses in renal parenchyma
15	Chiaudano.....	1921	Right	Intermittent pyuria and pain in right kidney	11 years	Well defined areas of leukoplakia scattered over whole pelvis; infected hydronephrosis
16	Corsdres.....	1923	15	F	Left	Renal colic	3 years	Hydronephrosis; island of flattened epithelium at the ureteropelvic junction, forming almost a plug in ureter
17	Crabtree.....	1920	40	M	Hematuria	Leukoplakia extending from pelvis 2½ inches down the ureter; no associated pathologic condition found
18	Cummings.....	1923	28	M	Left	Frequency and burning on urination	3 years	Vesical calculus and cystitis; leukoplakia of entire mucous membrane of pelvis
19	Ebstein.....	1882	20	F	Definite small raised areas of shiny mucous membrane; hydronephrosis and hydro-ureter
20	Ebstein.....	1882	48	..	Right	White shiny raised area of cornified epithelium in right pelvis; also pyelitis, ureteritis and pyelitis cystica
21	Franeke.....	1929	14	M	Right	Several years	Entire renal pelvis and ureter covered with leukoplakia; hydronephrosis; vesical calculus
22	Finkel.....	1909	Hydronephrosis; renal pelvis with that epithelium and found to contain many pear-like elements; old hydronephrosis and stones
23	Fuetterer.....	1905	Plaques of leukoplakia in renal pelvis; stone and adenocarcinoma

24	Hallé.....	1896	20	M	Bilateral	Incontinence at 4 years of age; cystitis at 22 years; passage of sand for 25 years; vesical calculus removed 18 months ago	5 years	Leukoplakia of right pelvis and both ureters; bilateral hydro-nephrosis
25	Hallé.....	1896	70	M	25 years (?)	Leukoplakia of both pelves and ureter
26	Hallé.....	1893
27	Himman.....	1922	37	F	Right	Passage of gravel during pregnancy
28	Himman, Kutzmann and Gibson	1923	38	M	Right	Nocturia (once or twice)	10 years	Pelvic mucous membrane was thick, white and irregular; colic- ous pyelonephritis One small area in renal pelvis showing the normal transitional epithelium gradually changing to the squamous type; calcu- lous hydronephrosis and chronic pyelonephritis Entire pelvic wall is covered with a thick wrinkled epidermoid sheet; hydronephrosis and chronic pyelonephritis Renal pelvis was filled with white scaly débris from leukoplakic membrane covering pelvic wall Dry shiny pearly wrinkled surface at ureteropelvic junction Nephrosis Epidermization of lower pelvis in a double kidney; pyo- nephrosis; stone in lower left ureter Nearly entire pelvic mucous membrane showed wide, confluent areas of thick, epidermizing membranous covering; hydro- nephrosis Large kidney, showing an infected hydronephrosis; pelvic mucosa had a covering of leukoplakia extending down the ureter; chronic diffuse pyelonephritis Cornification of calices; pelvis filled with squamous cell cari- noma; infected hydronephrosis Mucous membrane of posterior pelvic wall showed area of leuko- plakia; infected hydronephrosis Large patch of leukoplakia about ureteropelvic junction extend- ing to calices and ureter; tuberculosis Area of leukoplakia on posterior pelvic wall; hydronephrosis; In cystitis In renal pelvis at level of middle calyx was an area of leuko- plakia 2 inches (5 cm.) in diameter; tuberculosis; pyonephrosis; Superior calices and lower part of pelvis had a dull china-white covering; infected hydronephrosis and stone; ureteral stricture Renal pelvis and ureter showed longitudinal wrinkles and folds Most of pelvic mucosa covered by a skinlike formation; some of calices filled with atheromatous material; hydronephrosis; nephrolithiasis Whole pelvis thickened, leather-like and swollen; pelvis contained fatty, shiny cholesteatomatous material; leukoplakia; hydronephrosis; Pelvis covered with granulations; infection had destroyed leukoplakic covering; soft calculi and pyonephrosis Pelvis and cavity-like calices are covered with a whitish wrinkled thick parchment-like membrane; pyonephrosis Entire renal pelvis covered with leukoplakia; calculus; pyone- phrosis
29	Himman, Kutzmann and Gibson	1923	34	F	Right	Suprapubic distress	20 years
30	Israel.....	1901	50	F	Right	Puerperal cystitis	9 years
31	Israel.....	1901	49	F
32	Jura.....	1924	32	F	Left	Hematuria; pain in the left flank
33	Karo.....	1926	33	M	Right	Piercing pains in re- gion of the right kid- ney; frequency Pain in right lower quadrant; nausea and some frequency Pain in region of right kidney Occasional pain in right kidney Bladder distress	Many years 8 years 7 years 1½ months Several years 3 years 4 years 1 year 5 years 35 years 4 months 2 years 1½ years 3 years 6 months
34	Keane and Denis....	1928	37	F	Right
35	Kischensky.....	1901	32	F	Right
36	Kraul.....	1922	28	..	Right
37	Kretschmer.....	1922	40	F	Right
38	Kretschmer.....	1922	26	M	Right
39	Kretschmer.....	1928	34	F	Left
40	Kretschmer.....	1928	41	M	Left
41	Kretschmer.....	1928	61	M	Right
42	Klug.....	1922	40	F	Right
43	Klug.....	1922	39	M	Right
44	Kuetner.....	1929	35	M
45	Kutzmann.....	1929	26	F	Left
46	Lavonius.....	1913	40	F	Right

TABLE 2.—*Leukoplakia of the Renal Pelvis—Continued*

Case	Author	Date Age, Years Sex	Side	Initial Symptoms	Duration	Anatomy
47	Lavonius.....	1913 16 F	Right	1 year	A small part of the lower portion of renal pelvis shows a leukoplakia; renal tuberculosis
48	Lavonius.....	1913 47 F	Left	18 years	Entire renal pelvis and ureter involved with leukoplakia; chronic pyonephrosis
49	Lavonius.....	1913 29 M	Right	9 months	Patches of leukoplakia in the lower two calices; right renal tuberculosis
50	Lavonius.....	1913 22 F	Right	2 years	A small strip of leukoplakia, 2 cm. long, in upper part of renal pelvis; right renal tuberculosis
51	Leber.....	1883 4 mo. F	Renal papillae and calices covered with thick white epidermis; associated with leukoplakia of the eye; congenital
52	Leebé.....	1913 28 F	Right	Slight pain in iliac fossa; frequency	Greater part of pelvis changed to thick skin; marked infection; infected hydronephrosis
53	Liebenow.....	1891 7 M	Bilateral	Cystitis	3 years	Generalized leukoplakia of entire genito-urinary tract; urethral fistula, calculous pyelonephritis; cholesteatoma of under side of diaphragm
54	Mehon.....	1914 .. M	Multiple plaques in pelvis and down ureter
55	Patch.....	1929 47 M	Bilateral	Dysuria	16 years	Leukoplakia in both kidneys with squamous cell carcinoma in left kidney; leukoplakia and squamous cell carcinoma in bladder; severe urinary infection, calculus in right kidney and multiple calculi in bladder
56	Pedroso and Lequeret	1927 41 M	Left	Renal colic, hematuria and pyuria	3 years	Renal pelvis and calices entirely covered by a rough, pearly white membrane; pyelonephritis
57	Pedroso and Lequeret	1927 30 F	Right	Pain in right kidney region and later testis	3 years	Renal pelvis and calices were covered by a thick layer of a pearly white substance wrinkled in all directions; hydronephrosis
58	Pollack.....	1901 .. F	Formation of small islands of leukoplakia in renal pelvis
59	Rufin.....	1907 50 F	Left	5 years	Entire renal pelvis showed leukoplakia; stone and hydronephrosis
60	Reektenwald.....	1909 60 M	Left	Bladder trouble	7 months	Pelvis covered with silvery membrane; hydronephrosis and hydro-ureter
61	Rieley.....	1920 43 M	Right	Paroxysms of back-ache	22 years	Entire pelvis covered with leukoplakia; hydronephrosis and infection
62	Romilt.....	1922 25 M	Left	Persistent urinary fistula following pyelotomy	6 years	Mucous membrane of pelvis grayish white and shiny-like pearl; associated with foreign body and stone formation
63	Rona.....	1901 35 M	Left	Two thirds of left pelvis covered with thick pavement epithelium; stone in right kidney; hydronephrosis
64	Rona.....	1901 46 M	Right	Xerosis of right pelvis; squamous cell carcinoma of bladder; pyelonephritis
65	Spies.....	1915 54 F	Left	7 years	Calices showed leukoplakia; lower part of kidney showed an oxalate stone surrounded by a squamous cell carcinoma
66	Stoekmann.....	1902 .. F	Right	Acute cystitis	2 years	Plaques in urine diagnosed leukoplakia; cured with lavages of silver nitrate
67	Thomson-Walker....	1927 63 M	Right	Colic and lumbar pain	27 years	Pelvic lining showed leukoplakia which passed into squamous carcinoma with cell nests; calculous pyonephrosis

to this is Stockmann's and Beer's cases in which cornified epithelial plaques were found in the urine, causing some observers to consider the passage of these as pathognomonic of leukoplakia.

Nearly all patients complain of dysuria, burning on urination, frequency, urgency and similar urinary disturbances, all of which are due to the associated infection (pyelitis, pyelonephritis, pyonephrosis, cystitis and lithiasis), the presence of which may have persisted over many years. Lumbar pains and backache varying from the dull type to the acute renal colic are encountered. The latter has been thought to be due in some cases to small leukoplakic plaques moving down the ureter. The urine nearly always shows infection and pyuria. Hematuria occurred in twenty-four of the sixty-seven reported cases (35.8 per cent). It was found in eleven of forty cases of pyonephrosis and pyelonephritis, five of thirty-one of hydronephrosis, nine of twenty-four of stone, four of ten of tuberculosis and one of seven of malignant disease. While in this analysis hematuria is shown to be due probably to the existing associated condition, it should nevertheless be considered as a significant sign.

Careful urologic examination and study are imperative to determine the exact status of the urinary tract and for the diagnosis of the associated condition. The leukoplakic process, if confined only to the renal pelvis, will remain undiagnosed in most cases. Careful cystoscopic examination of the bladder may occasionally give a clue. Leukoplakia may be noted here, the observer finding the irregular plaque membranous formation, varying in luster from a dirty white to gray, raised from either a normal or an infected vesical mucous membrane. The silvery gray luster of these areas causes them to stand out from the adjacent tissues. Close observation will show no blood vessels coursing through these areas. The possibility of finding a leukoplakia should always be borne in mind in all long-standing and chronic cases of urinary infection, and a careful pathologic examination should be made of all material removed from the kidney at operation. This method of procedure would probably prove that leukoplakia of the renal pelvis was of more frequent occurrence.

Treatment.—Since it is not possible to diagnose leukoplakia of the renal pelvis as such, treatment must be directed toward the associated condition. The infectious process has usually destroyed the kidney beyond repair; if the condition is unilateral, nephrectomy is the procedure indicated. The relationship of leukoplakia to malignant disease (squamous cell carcinoma) should also be borne in mind when treatment is instituted. It has been found useless to treat these patients conservatively, because the associated condition has usually been present for a long period.

If there are any contraindications to surgical treatment, such palliative measures as pelvic lavage with a weak solution of silver nitrate or removal of the desquamating membrane by curettement may be instituted. Fulguration and application of radium has given only limited success in vesical cases. Stockmann reported a cure after twenty-one lavages of the renal pelvis with 5 per cent solution of silver nitrate.

SUMMARY

1. Leukoplakia of the renal pelvis is of importance because of its unknown etiology and pathogenesis, its difficulties in diagnosis and treatment and its relationship to malignant disease.

2. Leukoplakia signifies the formation of white patches on the mucous membranes, that is, an epidermization of the mucosa with keratinization and desquamation.

3. Leukoplakia of the renal pelvis is only relatively rare, sixty-seven cases being collected to date. This probably represents only a part of a number of cases unrecognized or not reported.

4. Leukoplakia of the renal pelvis is associated with a chronic urinary infection or lithiasis; hence the clinical picture is one of urinary infection and chronicity.

5. Leukoplakia of the renal pelvis occurs most frequently in the fourth decade of life, is found equally in both sexes and occurs equally in both kidneys.

6. There are two principal theories concerning the etiology of leukoplakia: (a) The process is one of metaplasia or adaptation and protection by cornification to a chronic irritative inflammatory environment. (b) Leukoplakia is of congenital origin, being due to misplaced embryonal cell rests from the primitive ectoderm.

7. The treatment is that employed for the associated condition, nephrectomy usually being carried out if the condition is unilateral. Palliative measures such as pelvic lavage have been used. Fulguration and radium have given limited success in vesical cases.

8. One new case of leukoplakia of the renal pelvis is reported.

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OXYGEN CONTENT OF BLOOD IN PATIENTS WITH VARICOSE VEINS*

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The pathogenesis of varicose veins and the concomitant abnormalities of the circulation are not clearly understood. My purpose in this paper is to record observations made in the course of study of the blood gases in a series of patients with apparent abnormalities of the veins of the extremities. Although these observations are insufficient for significant conclusions concerning the pathogenesis of conditions peculiar to varicose veins, they are sufficient for definite conclusions concerning certain fundamental facts that must be considered hereafter in similar studies.

Most of the observations on the gases of the blood of peripheral vessels have been made for normal persons, and usually the blood of the upper extremities has been studied. De Takáts, Quint, Tillotson and Crittenden¹ recently reported studies in which the carbon dioxide and oxygen contents of the blood of varices of the leg were compared with those of the blood from the cubital vein of the arm. They stated: "The carbon dioxide content of the varicose blood is definitely higher than that of the venous blood in the cubital vein of the same person. The reverse is true of the oxygen content." In normal subjects they found the same carbon dioxide content in samples of blood from the cubital and saphenous veins. The oxygen content of the blood from these veins was apparently assumed to be the same. Goldschmidt and Light² found marked differences in the carbon dioxide and oxygen content of samples of blood from closely adjacent veins of the forearm. They stated: "Closely adjacent veins of the forearm may exhibit differences in their content of blood gases. The carbon dioxide and oxygen contents of two bloods, drawn consecutively from the hand and bend of the elbow, may vary independently." They found that the dependent position of the arm, even with the development of venous engorgement had little effect on the average gaseous content of the

* Submitted for publication, May 21, 1929.

* From the Department of Surgery, Vanderbilt University.

1. De Takáts, Geza; Quint, H.; Tillotson, B. I., and Crittenden, P. J.: The Impairment of Circulation in the Varicose Extremity, *Arch. Surg.* **18**:671 (Feb.) 1929.

2. Goldschmidt, S., and Light, A. B.: A Comparison of the Gaseous Content of Blood from Veins of the Forearm and the Dorsal Surface of the Hand as Indicative of Blood Flow and Metabolic Differences in These Parts, *Am. J. Physiol.* **73**:127, 1925.

blood from the veins of the forearm. De Takáts and his co-workers did not state the position of their subjects when the samples of blood were drawn.

METHOD OF STUDY

The observations recorded in this paper were obtained from the study of several normal persons and ten subjects with varicose veins. In the patients with varicose veins the disease was limited to one extremity, except in two instances in which it was much more marked on one side. Patients with symmetrical disease were considered as unsuitable for this study. The extent of the clinical manifestations as regards the varicosities and ulceration is indicated in the individual protocols.

The same method of procedure was carried out when possible in each person studied. Samples of blood were drawn from the femoral, saphenous and superficial veins of the leg in both the recumbent and standing postures. If the patient was standing, an attempt was made to obtain the samples of blood as nearly simultaneously as possible; if this was impossible, it was attempted to have the patient stand for the same period of time when samples from the corresponding veins were withdrawn. Samples of venous blood were collected without stasis. Precautions against contact with air were observed. The blood gas analyses were performed with the Van Slyke-Neill manometric apparatus.

The study of the normal persons was only for the purpose of obtaining observations before the study of abnormal cases. The results obtained are not to be considered in the sense of establishment of a normal standard of blood gas content, but only for the purpose of determining the effect of position. In these persons, blood from the femoral veins only was analyzed. Only the observations on one normal subject are recorded in this paper; others studied gave similar results.

In the ten patients with varicose veins, samples of blood were withdrawn from the femoral veins; in two of these, no attempt was made to obtain blood from other localities. Samples were obtained from at least one other vein in the remaining instances. When the figure for the oxygen content of the blood from the saphenous vein or from one of the superficial veins of the lower part of the leg on the diseased side is given without the figure for a corresponding vein of the normal side, it is because the vein of the normal side could not be seen without the production of constriction which would vitiate the result. Six of the ten patients with varicose veins had ulcerations of the lower part of the leg, and one had had previous ulceration.

OBSERVATIONS

Since the effects of changes in posture were studied on the patients with varicose veins, similar studies were made on people without such disease. An example of such a study is given in table 1.

This table shows that the oxygen content falls rapidly when the patient stands, and rises when the patient again assumes the recumbent position.

CASE 1.—J. W., a colored man, aged 65, entered the hospital because of several small ulcers and many prominent veins on the lower part of the left leg. The left saphenous vein felt cordlike. Several veins of the lower part of the right leg were a little more prominent than normal. The left leg was slightly larger than the right. The patient had active pulmonary tuberculosis. The Wassermann reaction was positive.

Samples of blood were obtained from the femoral and saphenous veins and from superficial veins of the lower part of both legs. The results are given in table 2.

It is to be noted that the oxygen content of the venous blood from the femoral vein of the left or diseased side is higher than that on the opposite side. The oxygen content of the blood from the superficial veins of the lower part of the legs was slightly lower on the ulcerated side.

TABLE 1.—*The Effects on Content of Blood Gases of Changes in Posture in a Patient Without Varicose Veins; Sample of Blood from Right Femoral Vein*

Position	Carbon Dioxide Content, Volumes per Hundred Cc.	Oxygen Content, Volumes per Hundred Cc.	Saturation, Per Cent
Recumbent	49.96	15.89	
	14.33	85
	15.69	..
Upright for one minute	50.53	10.74	58
Upright for two minutes	7.23	39
Upright for two and one-half minutes... .	51.76	6.88	37
Recumbent for one minute	49.43	11.70	63

TABLE 2.—*Oxygen Content in Patient (J. W.) with Varicose Veins and Ulcers of the Left Leg*

Vein	Recumbent		Standing	
	Oxygen Content, Volumes, per Hundred Cubic Centimeters	Saturation, Per Cent	Oxygen Content, Volumes, per Hundred Cubic Centimeters	Saturation, Per Cent
Right femoral ..	8.40	52.7	Standing 5 minutes 5.28	32.2
Left femoral (diseased side)	8.64	54.2	Standing 6 minutes 7.70	48.3
Right saphenous	Standing 4 minutes 3.67	21.3
Left saphenous (diseased side) ...	11.34	71.2	Standing 5½ minutes 8.87	55.6
Lower part of the right leg ..	8.86	54.5	Standing 6 minutes 6.66	41.8
Lower part of the left leg (above ulcer)	Standing 3 minutes 6.66	38.0
Lower part of the left leg (above ulcer)	Standing 4 minutes 5.46	31.3

CASE 2.—B., a white man, aged 24, entered the hospital because of varicose veins and ulcers of the lower part of the left leg of about five years' duration. The ulcers were very superficial and the foot had a cyanotic appearance. The saphenous vein was easily visible. There was no immediate filling of the saphenous vein when the leg was suddenly lowered, with the saphenous opening occluded. The Wassermann reaction was positive.

Samples of blood were drawn from the femoral, saphenous and superficial veins of the lower part of the legs and of the ankles. The results are given in table 3.

It is to be seen that whereas the oxygen content of the blood from the femoral veins is slightly lower on the diseased side, it is higher in

the saphenous vein of this leg. As was true of the previous case, the oxygen content is lower in the region of the ulcer than at a similar level on the opposite side.

CASE 3.—P., a white woman, aged 44, complained of varicose veins and a small ulcer of the lower part of the left leg. She first noticed the dilated veins fifteen years before entry, and the ulcer had been present for six months. The small ulcerated area was located just below a large bunch of varicose veins on the anterior surface of the middle third of the lower part of the left leg. The left saphenous vein was easily visible when the patient stood. The left saphenous

TABLE 3.—*Oxygen Content in Patient (B.) with Varicose Veins and Ulcers of the Left Leg*

Vein	Recumbent		Standing	
	Oxygen Content, Volumes, per Hundred Cubic Centimeters	Saturation, Per Cent	Oxygen Content, Volumes, per Hundred Cubic Centimeters	Saturation, Per Cent
Right femoral	14.66	77.0	6.04	31.7
Left femoral (diseased side).....	13.21	69.4	5.92	31.1
Right saphenous	8.53	44.8
Left saphenous (diseased side).....	13.87	72.9	11.23	59.3
Middle of the right leg.....	11.16	58.6
Middle of the right leg (above ulcer)....	7.26	38.1
Right ankle	11.10	58.3
Left ankle (below ulcer).....	6.88	35.1

TABLE 4.—*Oxygen Content in Patient (P.) with Varicose Veins and Ulcers*

Vein	Recumbent		Standing	
	Oxygen Content, Volumes, per Hundred Cubic Centimeters	Saturation, Per Cent	Oxygen Content, Volumes, per Hundred Cubic Centimeters	Saturation, Per Cent
Right femoral	13.88	73	10.90	60
Left femoral (diseased side).....	10.05	89	14.74	81
Left saphenous (diseased side).....	9.84	54
Lower part of the right leg.....	10.41	57
Lower part of the left leg (diseased side)	13.12	83	11.16	62

Twenty-six days after removing dilated veins and ulcer of the lower part of the left leg

Vein	Recumbent		Standing	
	Oxygen Content	Saturation	Oxygen Content	Saturation
Right femoral	11.34	63
Left femoral (diseased side).....	12.16	67

vein did not fill rapidly when the leg was suddenly lowered after being elevated, but the dilated veins of the lower part of the leg filled immediately. The left leg was larger than the right.

Samples of blood were drawn from the femoral and saphenous veins and veins of the lower part of the legs. The results are listed in table 4.

The oxygen content of the blood from the femoral veins was higher on the diseased side, and this difference was less marked after the dilated veins and the small ulcer had been removed from the lower part of the left leg. There was little difference in the oxygen content of samples obtained before operation from veins of the lower part of both legs.

CASE 4.—V. W. B., a colored man, aged about 35, entered the hospital because of varicose veins and ulcers of the right leg. The varicosities were first noticed sixteen years previously. The entire right leg and thigh were larger than the left. The ulcerated areas covered the greater part of the circumference of the leg. The Trendelenberg test indicated incompetence of the deeper veins. Several observers obtained different figures for the blood pressure in the two legs, but all agreed that it was higher on the diseased side. The Wassermann reaction was positive.

Samples of blood were drawn from veins at various levels on both legs. The results are given in table 5.

This table shows that the oxygen content is consistently higher in the extremity with varicose veins and ulcerations. Changes in posture caused little alteration in the oxygen content of the venous blood on the diseased side, and the figures were nearly the same whether the

TABLE 5.—Oxygen Content in Patient (V. W. B.) with Varicose Veins and Ulcers

Vein	Recumbent	Standing
	Oxygen Content, Volumes, per Hundred Cubic Centimeters	Oxygen Content, Volumes, per Hundred Cubic Centimeters
Right femoral (diseased side)	14 02	13 79
Left femoral	13 25	6 86
	7 15
Right saphenous, upper part of the thigh (diseased side).	15 00	12 05
	13 76
	13 79
Right saphenous, middle of the thigh (diseased side)	.	14 33
Right saphenous, at knee (diseased side)	15 32
Lower part of right leg (diseased side)	15 27
Lower part of the left leg	8 95
Right ankle (diseased side)	15 04
Left ankle	10 04

samples were taken from the upper or lower part of the leg. Due to the fact that the patient had a positive Wassermann reaction and also because the ulcers were not entirely characteristically varicose, there was some doubt as to the diagnosis. It can be stated with certainty, however, that there were many prominent dilated veins.

CASE 5.—H. H., a white man, aged 30, entered the hospital because of claw feet. It was noted on examination that he had several prominent veins on the anterior surface of the lower part of his left leg. Both feet had a cyanotic appearance. He had no ulceration at the site of the varicose veins. The two legs were apparently the same size.

With the patient standing, samples of blood were drawn from the right and left femoral veins and from veins at the level of the middle third of the lower part of both legs. The figures are given in table 6.

The blood from the femoral vein on the side with varicose veins had a higher oxygen content than that from the opposite side, but the reverse was true for the blood from the lower part of the legs.

CASE 6—J. W. T., a white man, aged about 50, entered the hospital because of an inguinal hernia. Some of the veins of the lower part of the right leg and the saphenous vein were prominent. There was no ulceration. Samples of blood were drawn from the two femoral veins with the patient standing. The oxygen content of the blood collected from the right femoral vein, on the diseased side, was 9.77 volumes per hundred cubic centimeters, while that from the left was 6.96 volumes. There was no marked difference in the size of the two legs.

CASE 7.—T. C., a colored woman, entered the hospital because of a small ulcer on the lower part of her left leg which appeared six weeks before, following a local injury. She had had several prominent veins in this area for nine years. There were no enlarged visible veins in the right leg. The left leg was slightly larger than the right.

While the patient stood, samples of blood were drawn from the femoral veins and from veins of the lower part of the legs. The figures are given in table 7.

TABLE 6—*Oxygen Content of the Blood in Patient (H. H.) with Varicose Veins Without Ulceration*

Vein	Standing	
	Oxygen Content, Volumes, per Hundred Cubic Centimeters	Saturation, per Cent
Right femoral	4.95	25
Left femoral (diseased side)	5.55	23
Lower part of the right leg	13.41	68
Lower part of the left leg (diseased side)	10.24	53

TABLE 7—*Oxygen Content of the Blood in Patient (T. C.) with Varicose Veins and Ulcer*

Vein	Oxygen Con- tent, Volumes, per Hundred Cubic Centimeters
Right femoral	10.43
Left femoral (diseased side)	13.97
Lower part of the right leg	5.49
Lower part of the left leg (diseased side)	5.49

The oxygen content of the femoral venous blood was higher on the side with varicose veins. The content of the blood from the lower part of the leg was the same on both sides.

CASE 8—A colored woman, aged 20, had a localized patch of dilated veins at the posterior surface of the left knee. There were no markedly dilated veins of the lower part of the legs and no ulceration. Samples of blood were drawn from the two femoral veins with the patient lying down. The oxygen content of the blood from the right femoral vein was 10.26 volumes per hundred cubic centimeters and that of the left (diseased side), 10.68 volumes. The oxygen content of the blood from one of the dilated veins with the patient standing was 11.52 volumes.

CASE 9.—W. L., a white man, aged 59, entered the hospital because of varicose veins of the right leg of fifteen years' duration. He also had a small ulcer just above the right ankle. The right leg was definitely larger than the left. There had been previously a large ulcerated area on this leg, and the area was markedly

discolored and hard at the time of examination. The saphenous vein was enlarged and hardened. A large mass of veins was easily seen just above the discolored area. With the patient lying down, the oxygen content of the right femoral vein (diseased side) was 11.1 volumes per hundred cubic centimeters, and that of the left (apparently entirely normal side) 10.2 volumes. The oxygen content of the blood from one of the dilated veins above the ulcer was 16.14 volumes per hundred cubic centimeters, and from a dilated vein on the right foot distal to ulceration it was 16.32 volumes. Blood could not be obtained from the small veins of the left foot and leg. Corrected venous pressures obtained with a citrate monometer showed the following readings for a dilated vein of right leg: with the patient standing, 32 cm. of water; with the patient recumbent, 17 cm. of water.

CASE 10.—J. E. L., aged 65, entered the hospital because of ulcers and swelling of the lower part of the right leg. He first noticed large tortuous veins on the

TABLE 8.—*Oxygen Content of the Blood in Patient (J. E. L.) with Thrombosis of the Inferior Vena Cava*

Vein	Recumbent		Standing	
	Oxygen Content, Volumes, per Hundred Cubic Centimeters	Saturation, Per Cent	Oxygen Content, Volumes, per Hundred Cubic Centimeters	Saturation, Per Cent
Right femoral	11.80	78.0	Standing 12 minutes 5.72	37.8
Left femoral	6.43	42.5	Standing 5 minutes 3.33	22.0
Lower part of the right leg.....	12.34	82.0	Standing 4 minutes 9.89	63.5
Lower part of the left leg.....	8.34	53.0	Standing 2 minutes 8.82	57.0
Repeat observation			Standing 4 minutes	
Lower part of the left leg.....	6.85	45.0
Repeat observation			Standing 3 minutes	
Lower part of the left leg.....	6.67	41.0
Repeat observation			Standing 10 minutes	
Vein above umbilicus.....	12.04	80.0	4.05	27.0
Left circumflex	11.09	74.0
Right femoral artery.....	13.95	92.0
Left femoral artery.....	14.55

lower part of the right leg, thirty-five years previously. During the past fifteen years, he had many ulcers of this leg, which disappeared and reappeared frequently. The right leg became quite swollen about six days prior to his admission to the hospital. Eighteen years before, prominent veins on the abdomen and lower part of the chest were noticed, and ten years before, the veins of the lower part of the left leg were thought to be enlarged. Several ulcers which healed rapidly appeared during this time on the left leg.

On examination, many prominent veins were seen over the lower part of the chest and abdomen. The direction of the blood stream in these veins was upward. Phenolsulphonphthalein injected into a vein of the lower leg could be recovered almost immediately from one of the dilated veins in the region of the umbilicus. There were many prominent veins of the lower part of both legs. On the left leg the scars of healed ulcers were seen, but there were no open areas. There were several open ulcers of the lower part of the right leg and a large area of hyperkeratosis in the region of the internal malleolus. The right saphenous vein felt cordlike. A diagnosis of thrombosis of the inferior vena cava was made.

The results of the analyses on various samples of blood are given in table 8.

This table shows that the venous blood from the extremity with the larger varicose veins and the ulcerations had a higher oxygen content than the opposite side.

To summarize briefly, in nine of the ten cases observed, the oxygen content of the blood from the femoral veins was higher on the diseased side or more diseased side than on the opposite side. This relationship held in both the standing and the recumbent postures. Changing from the recumbent to the standing position resulted in a smaller drop in the oxygen content of the diseased side than in that of the normal side. In the instances in which it was determined, the oxygen content of the blood from the saphenous vein was higher on the diseased side. No definite relationship seems to hold between the oxygen content of the blood of the dilated veins of the lower part of the leg and similarly located normal veins of the opposite leg, but the impression is gained that the oxygen content is lower on the diseased side when there is no ulceration and usually higher when there is ulceration. More cases will have to be studied in order to determine this point.

SUMMARY

1. The oxygen content of the venous blood of the femoral vein is highest when the patient is in the recumbent posture and decreases rapidly when the upright position is assumed.

2. In patients with unilateral varicose veins of the lower extremities, the venous oxygen content is higher in the femoral vein of the diseased side. This difference is usually accentuated when ulceration is present. Changes in posture cause less alteration in the venous oxygen content of the diseased side. Practically the same statements may be made regarding the oxygen content of the blood of the saphenous vein.

3. When ulceration is not present, it may be stated, in general, that the venous oxygen content of varicose veins of the lower part of one extremity is lower than that of similarly placed normal veins of the opposite extremity. However, when ulceration and infection are superimposed on the varicose veins, the oxygen content is usually higher on the diseased side.

4. Studies on one case of thrombosis of the inferior vena cava with prominent veins of the lower extremities revealed data similar to those obtained in the other cases with varicose veins.

5. The observations suggest that the total flow of blood through a leg with varicose veins is increased.

CARCINOMA OF THE COLON

INTRAPERITONEAL VACCINATION BY MIXED VACCINE OF COLON
BACILLI AND STREPTOCOCCI *

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Peritonitis is an urgent potentiality in any surgical maneuver for a malignant condition of the large bowel. The reasons for this group themselves mainly under three headings: (1) the peculiar conformation of the large bowel, which differs widely from the small intestine, both anatomically and physiologically; (2) the marked permeability of the large bowel when attacked by malignant disease, due either to its peculiar structure or to mucosal injury produced by large ulcerating carcinomas, and (3) the debilitation, dehydration and generally lowered resistance of patients who harbor neoplasms.

A glance at mortality statistics shows the necessity and desirability of adopting any measure which will, even in a small degree, tend to obviate peritoneal contamination, and it was with this in view that the isolation and individualization of cases of diseases of the colon at the Mayo Clinic were undertaken two years ago. This formation of a colonic unit has permitted us to adopt uniform measures in all cases as well as to study in detail the different types, the situation, the grades of malignancy and the technical procedures applicable to each. It has urged the adoption of numerous measures as well as the abandonment of many steps hitherto deemed satisfactory in our service. Among the details which have contributed in some measure to the reduction of mortality, and which have assured a more satisfactory outcome, has been the introduction as a routine in these cases of intraperitoneal vaccine of colon bacilli and streptococci. We believe this measure has given sufficient satisfaction to merit our reporting its employment in a series of sixty cases in which the patients were treated between June 1 and Nov. 6, 1928.

Although this is too small a series to allow us to assert dogmatically that vaccination is likely to prove of extensive benefit in malignant conditions of the colon treated surgically, we believe that as an adjuvant

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to surgical procedures and as a step in the preliminary preparation of patients for radical extirpation of malignant growths, peritoneal vaccination has marked value. Because, attending its use, there has been lessening of the postoperative reaction, a smoother convalescence and lowering of actual operative mortality, it commends itself to open minded criticism and trial before condemnation.

Herrmann¹ deserves great credit for pointing out the importance of the route by which protective vaccination may be carried out against gross fecal soiling and for working out methods of vaccination which are clinically adaptable. The reported work hardly does his thesis justice in that it is but a brief survey of extensive experimentation to establish ways and means of producing peritoneal immunity. Herrmann and others suggested that the exudate of peritonitis is a protective mechanism against the spread of bacteria and their toxins. He noted that if vaccination was seemingly complete, peritonitis did not appear. Similarly, varying gradations of vaccination resulted in varying amounts of fibrinous deposit and of exudation onto the peritoneum. David² also noted that when a transudate was formed in the peritoneal cavity of dogs, as by injection of hypertonic solution of dextrose, the absorption of diphtheria antitoxin was augmented, whereas in the presence of peritonitis, its absorption was decidedly retarded.

Métalnikov and Toumanoff,³ by injecting bacterial cultures or carmine into the peritoneal cavities of guinea-pigs, found early response on the part of the microphages; the maximal response occurred in three hours, but the proportion of macrophages was highest on the third day after injection, and the proportion of lymphocytes was highest on the fifth day. Phagocytosis clearly was manifested earlier in vaccinated than in nonvaccinated animals.

Kittinger,⁴ in twenty-six cases in which there was a gangrenous or perforated appendix and in two cases of strangulated hernia, in patients ranging in age from 4 to 86 years, poured from 50 to 150 cc. of colon bacilli and mixed culture filtrates into the peritoneal cavity after the necessary surgical procedure and made a primary abdominal closure. All of the patients lived.

1. Herrmann, S. F.: *Experimental Peritonitis and Peritoneal Immunity*, Arch. Surg., to be published.

2. David, V. C.: *Peritonitis; an Experimental Study*, Surg. Gynec. Obst. 45:287, 1927. David, V. C., and Sparks, J. L.: *The Peritoneum as Related to Peritonitis*, Ann. Surg. 88:672, 1928.

3. Métalnikov, S., and Toumanoff, K.: *Réaction des cellules et phagocytose chez le cobaye normal et immunisé*, Ann. de l'inst. Pasteur 39:909, 1925.

4. Kittinger, Alois: *Die Behandlung der eitrigen Peritonitis mit keimfreien Koli- und Mischkulturfiltraten (Antivirus)*, Wien. klin. Wchnschr. 40:997, 1927.

Steinberg and Goldblatt,⁵ in March, 1927, noted that after injection intraperitoneally of gum tragacanth and colon bacilli into animals, bacteremia did not occur, but peritonitis developed and death followed; with the injection of colon bacilli alone these organisms appeared in the lymph and blood stream. They interpreted these data as meaning that the peritonitis is the serious part of the process. Later experiments by them⁶ (January, 1928) tend to show that subcutaneous vaccination against such peritonitis is as satisfactory as vaccination by the intraperitoneal route. Herrmann's work tends to refute this hypothesis, and he demonstrates clearly not only the importance of the intraperitoneal route of vaccination, but the greater importance of using a mixed culture of colon bacilli and streptococci isolated from the heart's blood of animals that have died of peritonitis.

As early as 1921, Draper⁷ advocated the use of an antiserum against these two organisms. At the time of colectomy on patients at Trenton, he isolated streptococci and colon bacilli from the mesenteric lymph nodes of patients. Horses were immunized with these two bacteria, and patients were given from eight to ten injections of the horse serum over a period of a month with "definite decrease in mortality." In a recent personal communication, he stated that this work has not been continued.

Popesco-Combiesco⁸ recently demonstrated that extracts of platelets injected into rabbits immunized against cholera vibrio prevented cholera peritonitis. Mikulicz attempted intraperitoneal vaccination with colon bacilli but because of severe reaction to the patient, abandoned the method after three or four attempts. One of us (F. R.) had suggested repeatedly that vaccination of patients against peritonitis before operations on the colon had great potential value. It remained but to work out methods. Herrmann's experiments seemed so clearcut that we felt justified in attempting a similar procedure in patients who were to have resections of the colon for malignant conditions. The first vaccine used was prepared from human fecal strains of colon bacilli and strep-

5. Steinberg, Bernhard; and Ecker, E. E.: The Effect of Antiserum Against the Soluble Toxic Substance of *Bacillus Coli* in *Bacillus Coli* Peritonitis, *J. Exper. Med.* **43**:443, 1926. Steinberg, Bernhard; and Goldblatt, Harry: Studies on Peritonitis: I. Production of Experimental Peritonitis and Survival Following Intraperitoneal Injection of *Bacillus Coli*, *Arch. Int. Med.* **39**:446 (March) 1927.

6. Goldblatt, Harry; and Steinberg, Bernhard: Peritonitis: III. Active Immunization Against Experimental *B. Coli* Peritonitis, *Arch. Int. Med.* **41**:42 (Jan.) 1928.

7. Draper, J. W.: The Use of a Colon-Streptococcus and Anti-Serum as a Pre-Operation Measure, *Proc. Soc. Exper. Biol. & Med.* **19**:243, 1921-1922.

8. Popesco-Combiesco, Cornelia: Action préventive vis-a-vis de la péritonite vibrionienne expérimentale de l'extrait de plaquettes sanguines de lapins immunisés contre le vibron cholérique, *Compt. rend. Soc. de biol.* **97**:1001, 1927.

tococci isolated from the heart's blood of these animals after mass feces had been instilled in their peritoneal cavities. Similar strains were isolated later from patients who died with peritonitis, and most of the patients whose cases form the basis of this report received vaccine prepared from these strains of human origin. Vaccines were prepared separately from each of these organisms, and later a mixed suspension in sodium chloride was made with a density of about 1,000,000,000 organisms for each cubic centimeter. The organisms were isolated by means of a blood agar plate, and after isolation they were grown in dextrose-brain broth (Rosenow) or pancreatic-digest broth. Twenty-five hundredths of a cubic centimeter of this vaccine made up to 1 cc. with physiologic solution of sodium chloride was given subcutaneously one week before the anticipated date of operation. If an unusual reaction

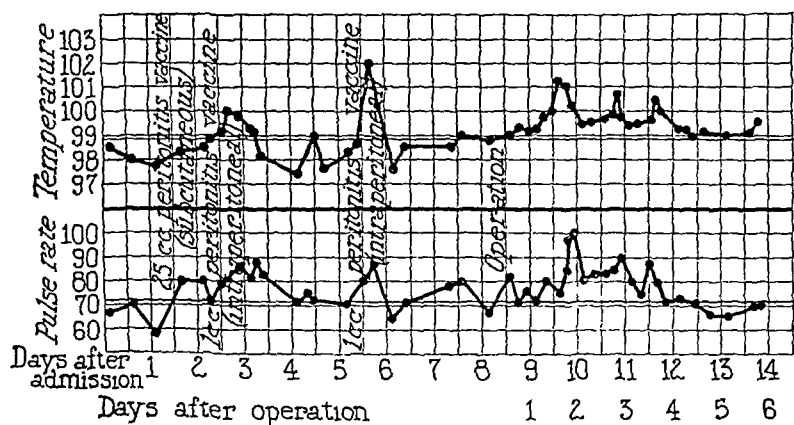


Chart 1.—Temperature chart of patient who had had two injections of intraperitoneal vaccine. Record for six days following ileocolostomy.

did not occur, 1 cc. of this vaccine in 10 cc. of the solution was injected intraperitoneally the next day. After an interval of two days, a similar injection was given; two days of rest followed, and then operation was performed.

Reactions following intraperitoneal injections all have been similar (charts 1 to 4); they are fairly severe and include rise in fever to as high as 103.5 F. within from two to four hours after the injection, diffuse abdominal soreness and tenderness, short jabbing abdominal pains, some distention, occasional chills and an invariable general leukocytosis. In from twelve to twenty-four hours this reaction subsides, a feeling of general well being prevails and often the entire blood picture improves.

The reaction from the second injection is almost invariably lighter (table 1).

Three of the sixty patients who received this vaccine in the manner described, together with the other preoperative measures described elsewhere, and who underwent the various surgical procedures (table 2) were found at necropsy to have had peritonitis. These three do not

TABLE 1—*Reaction to Vaccine*

Case	Before Vaccine			After Vaccine			
	Hemoglobin, Per Cent	Erythro- cytes, Millions	Leuko- cytes, Thousands	Hemoglobin, Per Cent	Erythro- cytes, Millions	Leukoocytes, Thousands	Tem- perature, F
1	65	3.58 *	10.0	73	4.72	14.2	103.0
2	48	3.15	6.6	60	3.92	13.2	101.5
						10.0	102.0
3	40	2.76	7.6	40	3.09	16.9	101.0
4	46		7.2	65		15.6	101.2
5	65	3.88	11.6	80	4.24	17.3	101.0
6	79	4.59	10.6	83	5.00	13.5	100.5
7	65	3.89	8.8	75	4.52	14.5	101.2
8	76	4.22	11.2	78	4.70	18.6	103.0
9	53	3.71	4.5	63	4.19	6.6	102.5

* Ileocolostomy

TABLE 2—*Operations After Treatment by Vaccine*

Patients	Lesion	Site	Surgical Procedures
5	Carcinoma	Cecum	First stage, ileocolostomy, second stage, hemicolectomy
4	Carcinoma	Ascending colon	First stage, ileocolostomy, second stage hemicolectomy
3	Carcinoma	Hepatic flexure	First stage, ileocolostomy, second stage, hemicolectomy
1	Sarcoma	Hepatic flexure	First stage, ileocolostomy, second stage, hemicolectomy
6	Carcinoma	Transverse colon	Obstructive resection (first and second stage Mikulicz)
1	Carcinoma	Transverse colon	Exploration
2	Carcinoma	Transverse colon	First and second stage Mikulicz and appendicostomy
1	Carcinoma	Transverse colon	First and second stage Mikulicz and partial gastrectomy
1	Carcinoma	Splenic flexure	First and second stage Mikulicz
1	Carcinoma	Splenic flexure	Colostomy
1	Carcinoma	Descending colon	First and second stage Mikulicz
1	Carcinoma	Descending colon	Colostomy and aseptic resection with anastomosis over Rankin clamp
1	Carcinoma	Descending colon	First stage, colostomy, second stage resection
1	Carcinoma	Sigmoid colon	Obstructive resection
3	Carcinoma	Sigmoid colon	First stage, colostomy, second stage, anterior resection with anastomosis
2	Carcinoma	Sigmoid colon	Exploration
1	Carcinoma	Sigmoid colon	Cecostomy, resection, and anastomosis
13	Carcinoma	Rectosigmoid colon	Procedures included combined abdominopereineal resection and colostomy, colostomy and resection, cecostomy, resection and anastomosis, and first stage, colostomy, second stage, resection
9	Carcinoma	Rectum	First stage, colostomy, second stage, posterior resection
1	Carcinoma	Ileum	Resection and end-to-end anastomosis
1	Malfunctioning ileocolostomy and cecostomy	Sigmoid colon	Cutting off and repairing
1	Chronic ulcerative colitis	Colon	Exploration and biopsy

embrace the total mortality in this group of cases, but it is noteworthy that in only three cases was there fatal peritonitis.

In the control group of sixty cases the lesions were located in the same segments of the colon as those in which the lesions were found

in the group which received vaccine, and the patients were operated on under the same conditions by the same surgeons. Of these fourteen died, a mortality of 23 per cent as against 5 per cent in the vaccinated cases.

The lowering of the mortality by 18 per cent in this series, while perhaps not attributable entirely to the vaccine, recommends it as a likely factor. The ages of the patients who received vaccine were as follows: four in the fourth decade, fourteen in the fifth decade, eighteen in the sixth decade, thirteen in the seventh decade and six in the eighth decade. The ages of the patients who did not receive vaccine were: seven in the fourth decade, fifteen in the fifth decade, seventeen in the sixth decade, fifteen in the seventh decade and six in the eighth decade.

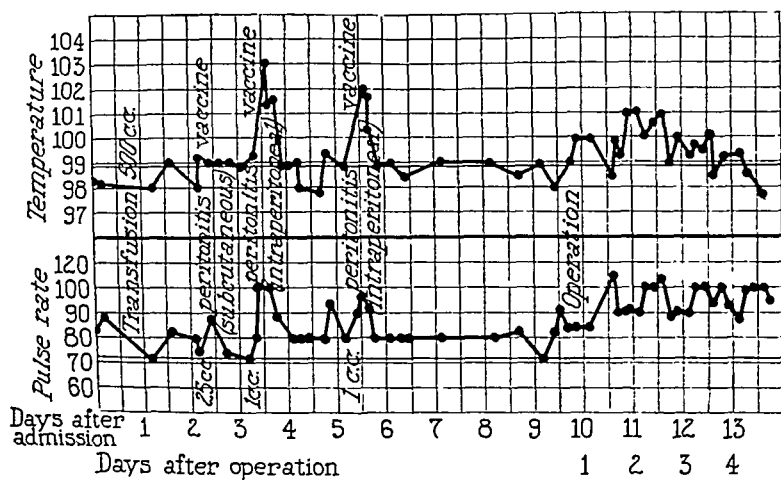


Chart 2.—Temperature chart of patient who had had two injections of intra-peritoneal vaccine. Course following first and second stage Mikulicz operation for obstructive carcinoma of the transverse colon.

Postoperative reactions, as measured by a rise in temperature, were greater in the nonvaccinated than in the vaccinated group. With the exception of one case in which the temperature rose to 105 F., the highest fever attained in the vaccinated group was 103 F. The average duration of fever after operation in the vaccinated cases, including three cases in which fever persisted for eighteen, nineteen and twenty days, respectively, was four and nine-tenths days. In several cases the maximal rise of temperature after resection was as low as 99.5 F. With the exception of one case in which the temperature rose to 106 F., the highest fever attained in the unvaccinated group was 105.5 F. The latter temperature occurred in several cases. In several cases the low level of 101 F. was attained as the maximal rise in temperature after resection. The average duration of fever after operation in the

group of cases in which vaccine was not given, omitting one case in which fever persisted thirty-five days, and another in which it continued for many weeks, was ten days. The groups include patients with lesions of all parts of the colon and rectum, one patient with carcinoma of the ileum and several patients who underwent resections for mechanical or adhesive obstruction.

There were seven patients with carcinoma of the cecum, four with carcinoma of the ascending colon, three with carcinoma of the hepatic flexure, one with sarcoma of the hepatic flexure, ten with carcinoma of the transverse colon, two with carcinoma of the splenic flexure, three with carcinoma of the descending colon, nine with carcinoma of the sigmoid, twelve with carcinoma of the rectosigmoid, six with carcinoma of the rectum, one with carcinoma of the ileum, one with a

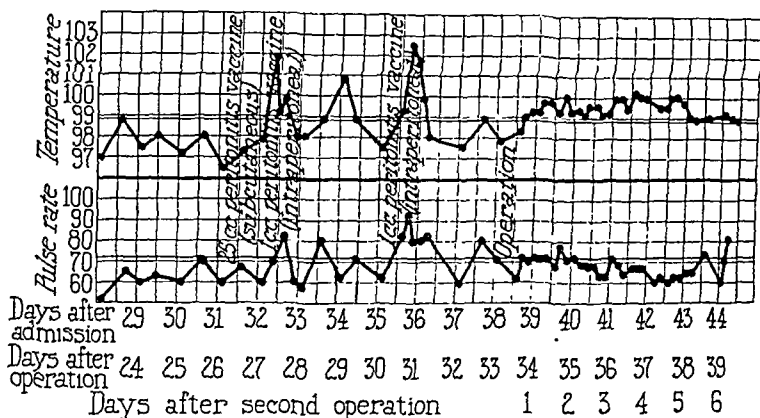


Chart 3.—Temperature chart of patient who had had colostomy and combined anterior and posterior resection for rectosigmoidal carcinoma after two injections of intraperitoneal vaccine.

malfunctioning ileocolostomy and cecosigmoidostomy, and one with chronic ulcerative colitis.

The group of patients who died following resection of the colon, after having had intraperitoneal vaccination, was small. Although the three cases which we discuss briefly do not represent the whole mortality in this series, they represent the total mortality among those patients who had peritonitis.

One patient, a man, aged 40, had an ileocolostomy for carcinoma of the cecum and ascending colon and died on the twelfth day from general peritonitis and ileus. This man had a large, fixed tumor of the cecum which was adherent to the abdominal wall. The advisability of resecting this tumor at a subsequent stage was questionable because of its immobility. An aseptic anastomosis was carried out satisfactorily, and we believe that peritonitis came from the exploration of the growth.

The second case was that of a man, aged 31, with a colloid carcinoma of the rectum, on whom a combined abdominoperineal resection was performed in one stage. He died seven days later, with general peritonitis and pelvic cellulitis.

In the third case, there is a question as to the accuracy of the diagnosis of cause of death. This patient was a man, aged 68, who had carcinoma of the transverse colon for which a temporary colostomy proximal to it was done. He died seven days later, and it was found that he had exudative peritonitis, but he also had marked myocardial degeneration and arteriosclerosis graded 3. The postoperative convalescence was entirely uneventful until the sixth day, when he suddenly went into collapse with some pain in the chest, dyspnea, cyanosis and a thready, rapid pulse which led us to believe he might be the victim

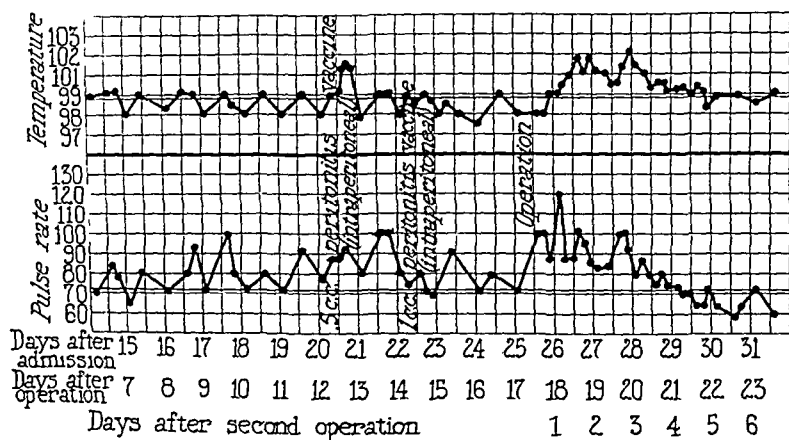


Chart 4.—Temperature chart of patient who had had resection of the right colon following injection of intraperitoneal vaccine. Rapid return to normal of pulse and temperature is shown.

of pulmonary embolus. He died twelve hours later. We count this death as one of peritonitis following colostomy, but believe that it is extremely doubtful whether the peritonitis actually was the cause.

Another case in this series in which the patient died is recorded because of the fact that a secondary operation for obstruction was necessary seven days after the resection, and at that time the abdomen was entirely free from any infection or contamination. This patient was a woman, aged 47, who had had a rectosigmoidal carcinoma and on whom a combined two-stage abdominoperineal resection had been performed. The colostomy was done on July 23; the resection, on Aug. 9, 1928. The first day following resection, ileus developed and enterostomy was performed. A loop of small bowel was found to be hugely distended and obstructed from adhesion into the pelvis. Enterostomy for acute intestinal obstruction was then performed. It was

noted that the peritoneal cavity was clear of any infection, and it was felt that relief from obstruction would prove life saving; however, the patient died eight days later, and peritonitis was found at post-mortem examination. Unquestionably, this peritonitis came from the enterostomy.

Table 2 shows types of operations performed after patients had been vaccinated and had received other preoperative care. The procedures employed in cases of patients who did not have vaccine were similar, although in a number of instances operations thought to be accompanied by less risk were employed.

CONCLUSIONS

Intraperitoneal vaccination with colon bacilli and streptococci, as an adjunct to other preoperative measures, seems a valuable asset in the treatment of patients with malignant growths of the colon. In this series of sixty cases, there was a definite lowering of mortality from peritonitis.

Postoperative convalescence was noticeably smoother than in the similar group of cases used as controls.

The value of cooperative management in these cases is well established, and selection of patients for operation, of types of operation for individual patients and of methods of anesthesia are important factors in the surgical treatment of malignant conditions of the colon.

ACUTE OBSTRUCTION OF THE SMALL INTESTINE DUE TO A GALLSTONE

RECOVERY FOLLOWING OPERATION *

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Intestinal obstruction due to a large gallstone impacted in the lumen is rare enough to occasion considerable interest. The early recognition of the condition is of especial importance because of the dangers of delay in operation.

Courvoisier,¹ in 1890, collected 131 cases of obstruction due to a gallstone. Wagner² found a total of 334 cases on record in 1914.

In a study of 3,064 cases of intestinal obstruction, reported from seven hospitals in 1925,³ there were only 28 due to a gallstone. The most frequent causes were hernia, intussusception, carcinoma, adhesions, internal strangulation and volvulus.

The age at which obstruction from a gallstone usually occurred was between 50 and 70 years. It was more common in women, in whom the incidence was 191, than in men, in whom it was 71 (Wagner).

Gallstones may gain access to the intestinal tract by perforation from the gallbladder or by entrance from the common duct.

In 36 cases studied, Courvoisier found a fistula from the gallbladder into the duodenum in 25, into the ileum in 1, and into both the duodenum and the colon twice. In the remaining 7 cases, the gallstone evidently entered through the choledochus.

Perforation from the gallbladder may follow a primary inflammation with attachment to a viscus or the inflammation may start in the latter, as from a perforating ulcer of the duodenum.

Courvoisier described fistulas between the gallbladder and the pleura, the lungs, the female genitals, and passage of gallstones from the urinary bladder.

The site of incarceration of the gallstone is usually in the terminal ileum because of its small lumen. Hermann⁴ found in 145 cases that

* Submitted for publication, March 2, 1929.

1. Courvoisier, L. G.: *Beitrage zur Pathologie und Chirurgie der Gallerwege*, Leipzig, 1890, p. 101.

2. Wagner, Arthur: *Ileus durch Gallensteine*, *Deutsche Ztschr. f. Chir.* **130**:353, 1914.

3. Report from Annual Meeting of the British Medical Association, *Brit. M. J.* **2**:993 (Nov. 18) 1925.

4. Hermann, quoted by Wagner.

the point of obstruction was in the colon in 13 cases, the duodenum in 9, the jejunum in 30 and the remainder in the small intestine, chiefly the terminal portion.

Wagner reported a fatal case in which two separate perforations from the gallbladder into the duodenum were followed by attacks of ileus fifteen days apart, and operative removal of the gallstone during each attack.

Unusually large gallstones have reached the terminal ileum before incarceration. Rankin and McKeith⁵ reported one measuring 6.9 by 8.5 cm., Clement⁶ found one gallstone measuring 2½ by 1¼ inches (6.3 by 3.1 cm.). Bennett⁷ removed one at operation with the greatest circumference of 5½ inches (14 cm.) and weighing 636 grains (41.3 Gm.).

Large gallstones have passed spontaneously after severe symptoms of ileus. Coldren⁸ reported one 2 by 1 inches (5 by 2.5 cm.) in diameter, which passed after severe obstructive symptoms for one week, with recovery. A volvulus of the small intestine occurred above the gallstone obstruction in a case reported by Smith.⁹

The onset of symptoms is usually acute, with severe colic, persistent pain and vomiting. Moore¹⁰ observed that the pain may be more on the left side. Visible peristalsis may be observed. The vomitus usually contains bile at first, and then becomes fecal with the development of tympanites and other evidence of obstruction. The condition of the patient is usually good for the first few days.

Wagner stated that one may occasionally palpate the gallstone. Bonnacaze and Le Chaux¹¹ stated that a tumor may be felt with the patient under anesthesia, and that the symptoms of obstruction may be mild but persistent.

A roentgenogram of the abdomen may show distention of the small intestine, characteristic of obstruction, with the shadow of the gallstone, as in the case reported. Displacement of the colon may result from the distended loops of intestine. As a means of localizing the obstruction

5. Rankin, F., and McKeith: Gallstone Ileus, *Kentucky M. J.* **22**:236 (July) 1924.

6. Clement, G. H.: Intestinal Obstruction Due to Gallstones, *Canad. M. A. J.* **11**:262 (April) 1921.

7. Bennett, Charles: Obstruction of Small Intestine by Gallstones. *Brit. M. J.* **1**:565 (March 27) 1926.

8. Coldren, R. S.: Intestinal Obstruction by Gallstone, *Brit. M. J.* **1**:783 (May 1) 1926.

9. Smith, N. R.: Acute Intestinal Obstruction Due to a Gallstone, *Brit. M. J.* **2**:479 (Sept. 12) 1925.

10. Moore, G. A.: Gallstone Ileus, *Boston M. & S. J.* **192**:1051 (May 28) 1925.

11. Bonnacaze, J., and Le Chaux, A.: *Arch. d. mal. de l'app. digestif* **14**:201 (March) 1924; abstr., *J. A. M. A.* **82**:1821 (May 31) 1924.

in the small or large intestine, it may be advisable to use the roentgen rays following a barium enema. Although the symptoms may be suggestive, the diagnosis has rarely been made before operation.

The prognosis is good with early operation, since there is rarely early strangulation of the obstructed intestine. However, the mortality rate has always been high, due to late operation. Fourteen of twenty-eight cases were fatal.³

The treatment is immediate operation. Usually removal of the gallstone and closure of the intestine is all that is necessary. An enterotomy was done in twenty-five of twenty-eight cases, and an enterostomy in three.³

REPORT OF CASE

History.—J. D., a woman, aged 63, complained of acute pain in the epigastrium, vomiting, loss of appetite and some fever.

The onset began with sharp pains in the epigastrium one week before admission to the hospital. They were somewhat intermittent, but had been worse the previous night. There was radiation of the pain to the back. Nausea was severe with some vomiting of dark, bitter material increasing in severity the last two days.

There had been two previous similar attacks of pain, one fifteen years ago, and another, a year ago. There had been numerous mild attacks of pain and discomfort especially during the last year. The patient had never been jaundiced.

The bowel movements had been regular, with slight constipation the last two months. There were no clay-colored stools. The appetite was usually good. The patient had never noted that any special food caused distress. On admission to the hospital, she weighed 233 pounds (105.7 Kg.), showing a gain of 40 pounds (18.1 Kg.) in the last six months.

The patient had passed five or six small stones from the bladder, some during the last year. There was an occasional slight burning on urination, but no hematuria.

She had had pneumonia eighteen years ago, and had had smallpox when a child. There was no history of typhoid. An operation had been performed three years ago when the uterus was removed for a tumor.

She had had two children, both of whom were living and well. Her father died at 76 years of age with kidney trouble, and her mother at 76 with heart trouble. She had five brothers, who were well, and three sisters, who were dead.

Examination.—The woman was very obese and did not appear acutely ill. The abdomen was prominent and fat. Tenderness with some muscle spasm and rigidity was present over the region of the gallbladder, but no mass was palpable. The abdomen was not distended with gas. Otherwise the results of the examination were negative.

The pulse rate was from 96 to 108. The temperature was 100 F., increasing a little during three days of observation in the hospital.

The blood count showed: white blood cells, 11,800; hemoglobin, 70 per cent; red blood cells, 4,780,000. The blood pressure was 120 systolic and 58 diastolic. The urine was normal, except for a trace of albumin on the second day. An Ewald test-meal demonstrated free hydrochloric acid, 35; total acid, 40. The stools were negative. The van den Bergh test of the blood was negative on both the direct and the indirect reactions.

A roentgenogram of the region of the gallbladder showed a small spherical, dense shadow with a faint oval shadow about it (fig. 1 *A*). The roentgenologic diagnosis was that the outer fainter shadow was due to a thickened, enlarged gallbladder containing a stone, as shown by a central denser shadow. Roentgenograms of the kidneys were negative. There was a small area of density in the pelvic region suggesting a bladder stone.

The increasing severity of the symptoms with vomiting, and the roentgen observations, made it seem advisable to operate without further delay.

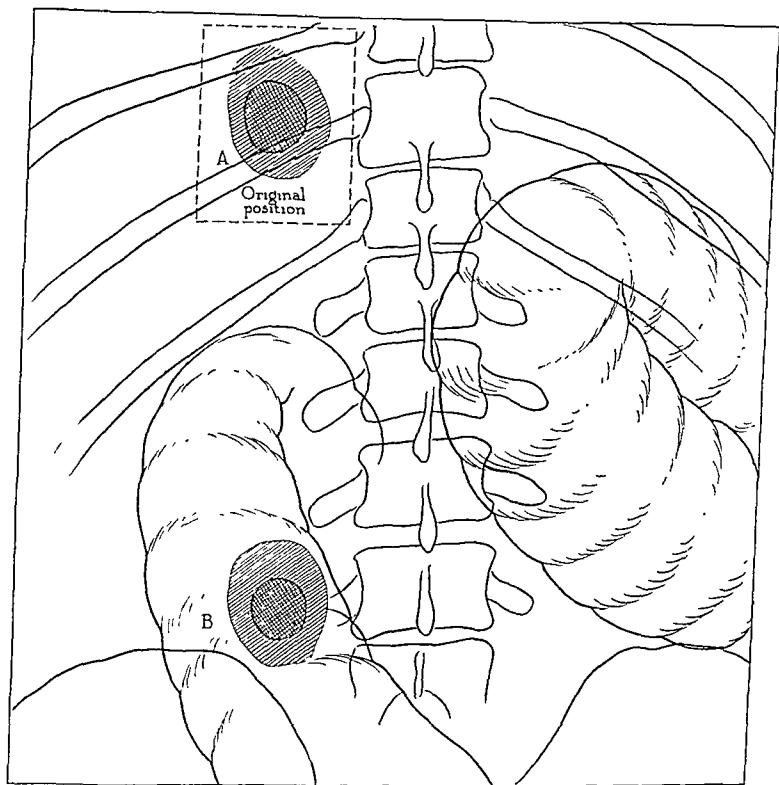


Fig. 1.—The insert *A* was made from a roentgenogram taken two days before operation. It shows the shadow of the suspected gallstone over the region of the gallbladder. The more dense central area was thought to be a gallstone, while the outer area of density resembled an enlarged thickened gallbladder. *B*, made from a roentgenogram taken eight days following operation, shows that the shadow had shifted downward. At a second operation a huge gallstone was found impacted in the terminal ileum, with complete intestinal obstruction. Several markedly dilated loops of small intestine are clearly shown in the roentgenogram.

First Operation.—Ethylene with some ether was given. The abdomen was explored as well as possible, considering the obesity. No abnormalities, apart from the gallbladder region, were found. The intestines were not distended, and the pancreas was normal. There was an acute inflammatory mass over the region

of the gallbladder formed by adhesions of the omentum to the liver and duodenum. This mass was hard and edematous, resembling a malignant induration.

The omentum was carefully separated from the liver, and a small friable, thickened gallbladder was opened. The first portion of the duodenum was found to be intimately adherent to the gallbladder with extensive inflammatory tissue. When they were separated, a large opening was observed over 4 cm. in diameter in the duodenum, freely discharging bile and a lacerated opening along the lower side of the gallbladder. Owing to the extensive adhesions and inflammation, the existence of a perforation before separation of these viscera could not be definitely

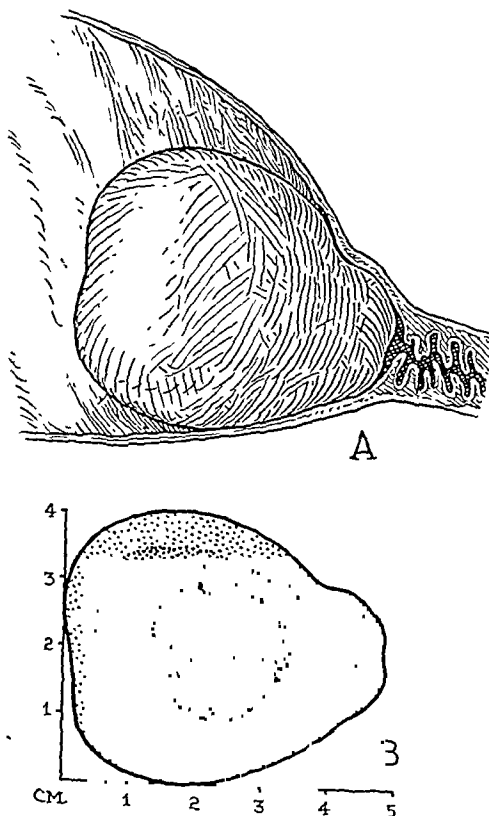


Fig. 2—*A* illustrates the large gallstone completely impacted in the terminal ileum. *B* was drawn from a roentgenogram of the gallstone after removal. It shows a dense central shadow and an outer lighter zone with two or three slightly shaded concentric layers. The stone measured 4 cm. by 4.8 cm. in diameter.

determined. The hole in the duodenum was closed transversely with layers of catgut and silk and covered with omentum.

The gallbladder was thickened, friable and severely lacerated. The cystic duct was narrowed and edematous. It admitted only a fine probe. The opening was enlarged, and the enlarged common duct was probed and palpated. The bed of the gallbladder in the liver was then searched for a gallstone, but none was found. Since the flow of bile from the common duct into the duodenum was not obstructed, and since the patient was not a good risk, due to her age and obesity,

no further exploration was done. The gallbladder was removed and the opening in the cystic duct closed with catgut. Drainage tubes were inserted and the abdomen was closed.

Postoperative Course.—For the first few days following the operation, convalescence was not unusual, although vomiting frequently occurred with small amounts of liquids. The stomach was washed, but vomiting persisted. After the first few days the stomach was washed more frequently, but gastric retention still persisted. On the sixth postoperative day, the gastric contents were observed to be foul smelling and of a brownish color. The stomach was washed every four hours day and night for the next two days. On the seventh day, there was copious drainage of bile from the wound and the amounts obtained from aspiration of the stomach were much lessened. On the eighth day, the patient seemed considerably weaker, and distention of the abdomen was noted for the first time.

During the entire postoperative course, plenty of fluids were given subcutaneously and by rectum. There had been little abdominal pain or complaint following the operation.

A roentgenogram of the abdomen was taken on the eighth postoperative day. There was a spherical shadow similar to that seen in the region of the gallbladder but it was now considerably lower on the right side, in the angle between the lumbar spine and the crest of the ilium (fig. 1 *B*). Distention of several loops of small bowel with gas, with widest measuring about 8 cm. was plainly seen. The stomach and colon were not distended. A diagnosis of obstruction of the terminal ileum by a gallstone was made.

Second Operation.—The second operation was done at once under local anesthesia. The region of the previous operation was prepared and walled off carefully, and the incision was made to the left of the umbilicus. Moderate distention of the jejunum and ileum with gas was present, with but little fluid content. The duodenojejunal angle was located and the intestine followed down until within 1 or 2 feet of the terminal ileum. Here the distended bowel terminated suddenly, due to a large gallstone, which was tightly impacted in the lumen. The bowel was completely collapsed below it (fig. 2 *A*).

A longitudinal incision was made and the gallstone removed. The intestine was not gangrenous and the opening was closed transversely with catgut and fine silk. There was a small amount of turbid exudate in the peritoneal cavity, but the region of the liver and bile ducts was not disturbed. Closure was done without drainage.

Postoperative Course.—Convalescence was uneventful and bile drainage stopped after ten days.

The microscopic sections of the gallbladder showed an acutely inflamed, greatly thickened wall. The gallstone was black and moderately soft on the surface. It measured 4 cm. by 4.8 cm. A roentgenogram of this stone showed a central spherical dense shadow and an outer, more oval lighter shadow (fig. 2 *B*). Several concentric outer layers were evident in this film, but not in those taken of the abdomen.

COMMENT

It is probable that the gallstone perforated shortly before the first operation, since the roentgenogram taken two days before showed the shadow in the region of the gallbladder. Vomiting and retention, which developed that day, were probably the result of the entrance of the large stone into the upper intestine. However, the stone probably did not

produce complete obstruction until the eighth postoperative day. Then it became completely impacted in the lumen of the narrow terminal ileum, and tympanites developed.

A roentgenogram was then taken of the abdomen, which showed marked distention of the small intestine and downward displacement of the shadow of the gallstone. This permitted a correct diagnosis.

At the first operation, the gallstone was thought to be only the central dense shadow surrounded by a thickened gallbladder, giving a faint shadow. There was no indication to strip the small intestine before exploring the indurated mass about the gallbladder, since there was no distention of the intestine. After the opening in the duodenum was closed, the bile ducts explored and the severely lacerated gallbladder removed, the condition of the patient did not justify prolonging the operation in further search for the gallstone.

The shadow interpreted in the first roentgenogram as the gallstone was only the denser core, which was apparently small enough to pass through the intestine. If it had been possible to determine that such a large gallstone had already perforated into the duodenum it would have been preferable to find and remove it without disturbing the inflammatory mass about the gallbladder.

CONCLUSIONS

1. A gallstone as a cause of intestinal obstruction should be considered with symptoms of inflammation of the gallbladder followed by those of intestinal obstruction.
2. Roentgenograms may show characteristic evidence of intestinal obstruction together with the shadow of the gallstone.
3. Early operation should be performed.

A REVIEW OF UROLOGIC SURGERY*

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KIDNEY

Anomalies.—Kimbrough¹ reported a case of carcinoma of a horse-shoe kidney occurring in a man, aged 35 years. Cystoscopic examination did not show anything of a pathologic nature in the bladder. A specimen from the left ureteral orifice was bloody, and one from the right was clear. Catheters were passed to the pelvis of the kidney without difficulty. A pyelogram revealed that the right ureter entered the pelvis laterally and was somewhat dilated. The calices pointed toward the median line and the pelvis was dilated. The left kidney was over the third and fourth lumbar vertebrae. During general examination a palpable mass was felt in the left side of the abdomen above the crest of the ilium. The mass was smooth, firm and slightly movable, and was posterior to the descending colon. It had an excursion of 1 cm. with respiration. The preoperative diagnosis was congenital anomaly, probably fused kidney.

At operation a large, fairly solid-feeling, smooth, walled-off mass about 10 cm. in diameter was exposed behind the posterior peritoneal layer, reaching upward under the ribs on the left side and over and across the median line below the stomach. The outer leaflet on the mesocolon of the descending colon was incised and the tumor exposed through this opening. The mass was dense and connected with the opposite kidney at the lower and inner portion by an isthmus of renal tissue. After considerable difficulty the tumor was exposed, and the pedicle and ureter were doubly clamped and divided. The isthmus

* Submitted for publication, Aug. 23, 1929.

1. Kimbrough, J. C.: Carcinoma of a Horseshoe Kidney, *Mil. Surgeon* 64: 91, 1929.

was divided and the left kidney was delivered. The kidney measured approximately 17 by 11 by 10 cm. The pathologic diagnosis was papillary adenocarcinoma.

[COMPILERS' NOTE.—Pathologic changes are more common in horseshoe kidneys than in the usual type of kidneys. Obstruction, infection and stone result from inefficient ureteral drainage. The formation of tumor, which is comparatively common in horseshoe kidney, apparently results from the same causes. Hellsten² found eight tumors in 107 cases of operative horseshoe kidney. Morley³ reported a case of papilloma of the renal pelvis causing hydronephrosis. Wolff⁴ reported a case of hypernephroma with extensive metastasis, even in the opposite renal segment. Haas⁵ described an unusual case in which the resected right kidney showed three different types of renal tumor. A hypernephroma about 8 cm. in diameter was found in the upper pole, an adenoma about 3 by 5 cm. was found in the lower third, and a small papilloma was found in the lower division of the pelvis. Several more recent cases of squamous cell tumors associated with calculi have been reported. In most of the published reports the cases are unusual in that the tumors are generally found in the right division of the horseshoe mass.]

Campbell⁶ presented a clinicopathologic study of nine cases of complete unilateral agenesis of the kidney found in 13,000 necropsies at Bellevue Hospital and one case presumably of this character observed clinically. In a series of 122,320 necropsies which Campbell reviewed, he found an incidence of one case of unilateral renal agenesis in 1,610 cases.

Clinically, apparent pathognomonic signs or symptoms of unilateral kidney are not present, and the condition is usually not suspected during life. The diagnosis is often not made until operation. Ransahoff stressed the surgical import of this condition; in 1912, he reviewed eleven cases in which, unknowingly, the only kidney had been removed or was otherwise surgically incapacitated. All the patients died promptly of uremia. Age is a factor of comparatively little importance. A person whose kidney is congenitally absent may expect as long a span of life as that for many patients on whom nephrectomy has been

2. Hellsten, O. T.: A Case of Hydronephrosis in a Horseshoe Kidney: Heminephrectomy, *Acta chir. Scandinav.* **59**:415, 1925-1926.

3. Morley, John: Case of Papilloma Causing Hydronephrosis in a Horseshoe Kidney, *Lancet* **1**:1617, 1910.

4. Wolff, T. R.: A Case of Hypernephroma in a Horseshoe Kidney, *Am. J. Urol.* **8**:627, 1912.

5. Haas, N. C.: Tumoren in Hufersennieren, *Ztschr. f. Urol.* **19**:81, 1925.

6. Campbell, M. F.: Congenital Absence of One Kidney: Unilateral Renal Agenesis, *Ann. Surg.* **88**:1039, 1928.

performed. Campbell noted, however, that in a third of the cases of this series that came to necropsy the patients died of renal failure.

Renal vessels were not found in seven of the series, and in two instances their presence was not recorded. In a series of thirty-nine cases of renal aplasia which Campbell reported elsewhere, a few were of degenerative type and unquestionably would be overlooked unless the atrophic vascular supply gave a clue. There was evidence of ureteral budding in only one of Campbell's cases. A fibrous thread left the bladder at the normal exit but was lost in the lumbar retroperitoneal fat. In none of his cases was a ureteral opening present on the affected side; dimpling was seen in four cases. Aplasia or agenesis of genital and reproductive organs is occasionally associated with renal agenesis. A unicorn uterus with rudimentary ovary and fallopian tube was found in two instances. In another case, the testicle on the involved right side was retroperitoneal and atrophic. The right seminal vesicle and vas deferens were also atrophic.

The solitary kidney must often bear an exceedingly heavy burden; in three of the cases a destroyed kidney was found at necropsy. In one case there was generalized infarction, in one case, acute suppurative focal nephritis, and in another case, a typically scarred kidney of chronic interstitial nephritis. All the patients died of uremia.

[COMPILERS' NOTE.—Attention is called again to the importance of bilateral renal investigation, if a surgical procedure on the kidney or ureter of one side is contemplated. Although the differentiation of solitary kidney and renal aplasia, atrophic pyelonephritis and occluded renal tuberculosis may be difficult, the practical point which can be demonstrated is that one kidney does not function. If this is demonstrated, it is sometimes necessary to change the character of the treatment of disease on the side which is carrying on the function.]

Hennessey⁷ reported a case of congenital solitary kidney. Three hundred seventy-two cases of congenital absence of the kidney have been reported in the literature. The frequency of this anomaly as indicated by necropsy reports is about one in 1,000 cases. The presence of two ureteral orifices does not always indicate that there are two kidneys. A ureteral orifice on the side of the renal aplasia was found in about 10 per cent of the cases. Associated genital anomalies occurred in about 33 per cent of the cases. The presence of genital anomalies should arouse suspicion of urinary dysplasia.

Pyelitis of Pregnancy.—Hofbauer⁸ stated that the cause of urinary obstruction in pregnant women is due to certain anatomic conditions

7. Hennessey, R. A.: Congenital Solitary Kidney, *J. Urol.* **21**:193, 1929.

8. Hofbauer, J. I.: Studies on the Etiology and the Treatment of Pyelitis in Pregnancy, *New England J. Med.* **198**:427, 1928.

in the portion of the ureter close to the bladder and in the trigonum vesicae. Hypertrophic changes in the musculature, associated with hyperplastic changes in the connective tissue, are essential factors in the narrowing of the lumen of the lower part of the pelvic portion of the ureter. The constriction is accentuated by an encircling ring resulting from hypertrophy of the ureteral sheath, and engorgement of the vessels in the mucosa and dextrorotation of the uterus may act as contributory factors.

It is common for pregnant women to have a moderate degree of hydro-ureter. The distal end of the ureteral dilatation usually lies at the level of the parametrium, the visible dilatation being associated with demonstrable delay in ureteral action. The hypertrophy of the trigonum accounts for the clinical phenomenon of residual urine in pregnant woman. Pugh noted that, in 100 apparently normal pregnant women examined between the seventh and ninth months of pregnancy, the ureters were sluggish in their action in 80 per cent of the cases. In practically every instance there was ureteral retention, mostly on the right side.

In six of fifty-five cases it was shown that there was definite lowering of the immunization power of the blood to the colon bacillus during pregnancy.

Histologic studies tend to substantiate the occurrence of involution processes within the ureteral wall, in analogy with the phenomena occurring in the uterus during the puerperium. Although after labor there is a gradual return of the renal pelvis and of the ureter to normal in uncomplicated cases, persistence of bacteria and of marked dilatation of the ureter is demonstrable in many women who had been treated for pyelitis during a preceding pregnancy. In the majority of these cases, the level above which the ureter has remained dilated corresponds to the parametrium. Stricture of the ureter may occasionally result from long-standing infection in the wall of the ureter during pregnancy.

Phaneuf⁹ stated that, clinically, pyelitis of pregnancy is frequently encountered in the average obstetric case, because of the high temperature usually accompanying the lesion and the subsequent reference of these patients to the hospital. In his experience the mortality in this condition is low; deaths were not recorded at the Carney Hospital. It has been his practice to use conservative treatment, almost ultraconservative in most cases. Lately the use of the indwelling catheter has been recommended to drain the ureter and the pelvis of the kidney. The value of this method is emphasized by the etiology, for it dilates the constricted area caused by the hypertrophy of the periureteral sheath.

9. Phaneuf, L. E.: Discussion, *New England J. Med.* **198**:437, 1928.

Irving¹⁰ reported that of 9,209 pregnant women, 204 had pyelitis, an incidence of about one in forty-five. In seven of the 204 patients, it was advisable to terminate pregnancy. The other patients recovered as the result of treatment which included the use of urinary antiseptics, rest in bed and forced fluids, or cystoscopy.

Crabtree,¹¹ during the last seven years, at the Boston Lying-In Hospital, has not known a case of pyelitis of pregnancy in which recovery from infection has taken place during pregnancy. Occasionally the urine cleared to bacilluria which persisted throughout pregnancy. In some instances, especially in the last weeks of pregnancy, the urine may become cloudy again and symptoms of fever recur. This is attributed to change of position of the fetus preceding the onset of delivery. Acquired immunity doubtless protects these patients and allows them to throw off the remnants of infection after the acute symptoms have subsided. If patients have acute symptoms, the contents of the pelvis are considerably greater than during the quiet stages of the disease previous to delivery. Bacilluria occurs frequently in pregnancy. In 200 cases of pregnancy, bacilluria was found in thirty-two.

Crabtree advised early cystoscopy as treatment of pyelitis of pregnancy, in the belief that reduction of overdistention and the clearing of a pelvis clogged with pus definitely hasten recovery.

[COMPILERS' NOTE.—The etiology of pyelitis of pregnancy has provoked much comment during the last few years. Carson, Pugh, and Corbus and Danforth have dealt intensively with the causal and therapeutic factors.

Stasis from organic changes in the ureteral musculature, from vascular engorgement, and from change in the anatomic relationships of the trigone, as well as the frequently lowered resistance of the patient to infections from the colon bacillus during pregnancy, has been the feature most often emphasized.

The fact has been established that pregnancy is associated with definite dilatation of the pelvis and ureter, which subsides to a greater or less degree during the first few months after the puerperium. Furthermore, it has been shown that a certain amount of residual pelvic and ureteral dilatation persists in most cases and thus renders the soil favorable for further infection, especially when the next pregnancy ensues.

The question of stricture as a result or as a cause of pyelonephritis of pregnancy is most elusive so far as its establishment as a pathologic fact is concerned. Corbus and Danforth stated that stricture is commonly associated.

10. Irving, F. C.: Discussion, *New England J. Med.* **198**:439, 1928.

11. Crabtree, E. G.: Discussion, *New England J. Med.* **198**:437, 1928.

Unquestionably treatment with diuretic and urinary antiseptic drugs must be of value in the hands of the average practitioner. Nevertheless there is a growing tendency not to expect too much from medical treatment or to continue it too long. The institution of cystoscopy with repeated renal lavage or permanent drainage by catheter is generally recognized as a better mode of treatment. The indwelling catheter occupies a questionable position in the minds of some urologists who believe that the prolonged employment of large catheters incites a form of ureteritis which may in itself be dangerous. However, accidents with the method are clinically rare, and there are increasing numbers of advocates of the large indwelling catheter as the ideal method of treatment for this distressing type of infection of the urinary tract.]

Seng¹² observed that, in pregnancy, there is constant rightsided ureteral dilatation, whereas hydronephrosis on the right side is only slightly less common. The left ureter and renal pelvis are not affected in a high percentage of cases. Bilateral hydro-ureter and hydronephrosis are common. In the multiparous woman these conditions occur earlier, more commonly, and in more marked degree than in the primipara. The inability of the renal pelvis and ureter to empty themselves within the normal time limits is an almost universal observation in the antepartum woman. Stasis persists in the postpartum woman but in a lesser degree over a prolonged period. In the apparently healthy pregnant and puerperal patient there is probably renal complication in the presence of pus and coliform organisms.

Tumor.—Kretschmer and Doehring¹³ stated that adenoma of the kidney is usually small, that it does not present clinical symptoms, and that it occurs most often in kidneys affected with interstitial nephritis. They reported a case of large benign adenoma, in which the kidney was removed and the patient was well without recurrence four years after operation.

The one constant symptom noted in a group of seventeen cases reviewed by Kretschmer was the presence of an abdominal tumor. Blood in the urine occurred in eight cases, pain in six cases and anemia in three cases. The tumor was on the right side in ten cases, and on the left side in four cases; in three cases the side was not designated.

The diagnosis of renal adenoma is difficult. A benign tumor is suggested if the mass in the hypochondrium is freely movable with respiration, painless and slow-growing. Roentgen examination may

12. Seng, M. I.: Dilatation of the Ureters and Renal Pelves in Pregnancy: Urological Study, *J. Urol.* **21**:475, 1929.

13. Kretschmer, H. L., and Doehring, Carl: Adenoma of the Kidney, *Surg. Gynec. Obst.* **48**:629, 1929.

show the mass. Unless the tumor encroaches on or compresses the renal pelvis, a negative pyelogram may be obtained, especially if the tumor originates from the lower pole. Examination of the urine may not reveal anything abnormal. If there is a sudden onset of gross bleeding, associated with pain in the region of the kidney and a palpable mass, a renal tumor is indicated.

Kretschmer and Randolph¹⁴ reported a case of spindle cell sarcoma in a man, aged 55 years. The patient had not been feeling well for several months and presented himself with epigastric pain occurring after meals, a mass in the left side, swelling in the left testicle and hemorrhoids. General examination revealed a hard, firm mass in the left side of the abdomen. This extended up to the ribs, across the median line, and down to a point just below the left anterior superior spine of the ilium. The tumor moved slightly with respiration. A mass of similar consistence and probably connected with the first mass was palpable just above the umbilicus. A good-sized varicocele was present on the left side. A differential test of function showed only a trace of dye returning from the left side. The pyelogram of the left side showed incomplete filling due to almost complete block of the renal pelvis; only a streak of the bromide appeared. The pyelogram of the right side was negative. A few erythrocytes and pus cells appeared in the urine from each side. A diagnosis was made of malignant tumor of the left kidney.

At operation a large mass, grayish-pink and moderately firm, which was adherent to the surrounding structures was found. The pedicle, which was hard and fibrous, was divided between clamps, and the mass was removed; the wound was closed after ligation of the pedicle. Large masses were noted both above and below the area from which the kidney was removed. These were not removed because of their extent and their proximity to the large vessels. The patient made a good operative recovery but died a year and seven months after operation. Necropsy revealed spindle cell sarcoma of the kidney.

It was pointed out that such a tumor is rare in the adult, but its occurrence in infants is not infrequent. In the reviewed cases in adults all but one of the patients were more than 34 years of age. Hematuria was present in only three cases. Varicocele and hemorrhoids are common accompaniments to malignant renal tumors. Loss of weight was reported in six cases. The preoperative diagnosis of sarcoma of the kidney as distinguished from other types of malignant neoplasms is practically impossible. Eleven cases from the literature were reviewed as to symptoms, and preoperative and operative data.

14. Kretschmer, H. L., and Randolph, H. S.: *Spindle-Celled Sarcoma of the Kidney in Adults*, *Ann. Surg.* 88:1033. 1928.

[COMPILERS' NOTE.—It is remarkable that, although the components of renal tumors are so varied in cellular characteristics, although there are so many conflicting opinions regarding the classification of such tumors from the standpoint of histogenesis, pure connective-tissue tumors of the sarcomatous type in adults should be encountered so seldom. The case reported by Kretschmer and Randolph is unusual in this respect. Fortunately, the differentiation of sarcoma, hypernephroma, and carcinoma is as yet largely academic. With the advent of newer forms of treatment, however, it will become necessary to attempt differentiation of tissue characteristics.]

Patch¹⁵ reviewed the literature and reported a case of squamous cell carcinoma of the renal pelvis associated with leukoplakia. He stated the belief that his case offered strong evidence in favor of transition between leukoplakia of the upper part of the urinary tract and squamous cell carcinoma of that region. One hundred and twenty-three cases of leukoplakia occurring in the kidneys, ureters and bladder, and 152 cases of squamous cell carcinoma in the kidneys, ureters and bladder were reported. The greater incidence of squamous cell carcinoma is probably because it is so difficult to detect. In thirty-six cases the growth occurred in the kidneys, in six in the ureter and in 110 in the bladder. There were seven vesical cases and three renal cases associated with leukoplakia; in two cases the leukoplakia was in the kidney and the carcinoma was in the bladder. Patch stated the belief that leukoplakia is the predecessor to squamous cell carcinoma and should be considered as a precancerous lesion.

[COMPILERS' NOTE.—Evidence is slowly accumulating that leukoplakia may be the forerunner of squamous cell carcinoma (Hinman and Gibson, Scholl, Kretschmer, von Borza). An analysis of sixty-seven cases of leukoplakia of the renal pelvis which were reviewed revealed the occurrence of seven squamous cell carcinomas and one adenocarcinoma, an incidence of 11.9 per cent (Kutzmann). Six of these occurred in the renal pelvis and two in the bladder. Patch showed that squamous cell carcinoma is only relatively rare in the urinary tract; 152 cases have been reported. There were thirteen cases of leukoplakia and squamous cell carcinoma coexisting in the kidney and bladder, a higher incidence than is surmised by many observers. Significance should be given to Hinman and Gibson's hypothesis that leukoplakia is the forerunner of squamous cell carcinoma. Leukoplakia, although a physiologicometaplastic process, may become a pathologic process in some cases. Its presence alone would tend to maintain an incurable state of chronic inflammation and irritation. The latter maintains con-

15. Patch, F. S.: The Association Between Leukoplakia and Squamous-Cell Carcinoma in the Upper Urinary Tract, *New England J. Med.* 200:423, 1929.

tinuous activity of epithelial proliferation as a protective process. Should this proliferative activity and destruction continue for a considerable period, the cells may undergo malignant change. Why a defensive process such as leukoplakia should be stimulated to undergo malignant change is one of the weaknesses of this hypothesis. However, the evidence submitted from time to time is becoming more conclusive. Patch demonstrated the transitional stages on repeated examinations, and although the changes were not definitely malignant, they were undoubtedly precancerous. Hinman, Kutzmann and Gibson were able to demonstrate in one of their cases, although not so definitely, an early papillary downgrowth with a beginning break in the basement membrane, suggestive of a malignant condition and hence considered precancerous. Kietschmer referred to leukoplakia, stone and chronic infection as the recognized predecessors of nonpapillary carcinoma of the renal pelvis. Von Boeza, in discussing squamous cell carcinoma considered constitutional factors, such as the endocrine system. Wolbach, in discussing Patch's report, reviewed some interesting pathologic data in the deficiency diseases or types of avitaminosis. In vitamin deficiency known as xerophthalmia or keratomalacia, extensive distribution of epithelial metaplasia was found in the conjunctiva, the ocular glands, the alimentary canal, the respiratory tract and the genito-urinary tract. It was noted that the epithelium became replaced by stratified keratinizing epithelium, strongly resembling leukoplakia. Wolbach found that a number of the experimental animals with this disease died of obstruction in the genito-urinary tract, caused by its occlusion and desquamated keratinized epithelial cells.]

Bugbee¹⁶ reported a case of leiomyoma of the kidney. His case is unique because of the fact that in the literature he was not able to find the report of a case in which the diagnosis was made during the life of the patient. The patient was a woman, aged 30 years, who had had a lump in the right side of the abdomen for some time. A pyelogram revealed that the kidney was associated with the mass. At operation the kidney and tumor were removed together. The tumor was in the lower pole of the kidney and was enclosed in a thin, fibrous capsule. The diagnosis was leiomyoma of the kidney. The patient recovered.

Creery¹⁷ observed pyrexia in two cases of malignant nephroma. Israel stated that of 146 operative cases of renal and suprarenal hypernephromas, fever was a symptom in 182 per cent., for a considerable

16 Bugbee, H. G. Leiomyoma of the Kidney. Report of a Case, *J. Urol.* **21**:363, 1929.

17 Creery, C. D. Pyrexia in Malignant Nephroma (Hypernephroma). *J. A. M. A.* **92**:1256 (April 13) 1929.

period in several instances it had been the only symptom noticed by the patient, who distinguished initial, intercurrent, and final fever, any one of which might be hectic, recurrent or hematuric. From a prognostic standpoint it was difficult to evaluate the fever, since several patients who exhibited pyrexia had remained well for a number of years after operation. On the other hand, it was at times associated with rapid growth or with extension of the tumor beyond the renal capsule, or with the development of metastasis. It also had occurred in cases in which none of these factors was present. Israel concluded that pyrexia was due to the formation in the tumor of specific pyrogenic substances. Creevy stated the belief that malignant nephroma should be considered whenever an obscure fever is present.

[COMPILERS' NOTE.—Fever, in cases of malignant nephroma, is sometimes septic in type, ranging from 105 to 98 F. On some occasions it may remain from 103 to 105 F. for a week at a time. Associated with the fever there may be severe pain along the course of the large nerves, especially the sciatic nerves. With removal of the kidney the temperature usually returns to normal, but in some instances, if there is recurrence of tumor (either local or in distant metastasis) the typical fever and nervous syndrome return. Fever recurring secondarily following operation is almost pathognomonic of metastasis.]

Speciale¹⁸ reported the case of a woman who, for six months, complained of pain in the left loin. Bimanual palpation revealed a soft, smooth, hypertrophied kidney. Urine from the left kidney obtained at cystoscopy contained pus. A diagnosis of pyonephrosis was made.

Examination of the kidney after nephrectomy revealed a malignant tumor. Nearly all of the kidney was composed of soft, grayish, friable tissue with hemorrhagic areas; the whole mass resembled tuberculous tissue. The microscopic aspect was that of perithelioma; many small, round formations, composed of pseudo-epithelial elements were distributed in concentric series around a central zone occupied by capillary blood vessels. Speciale stated the belief that the growth was an endothelioma which had developed from the cellular elements around the capillary blood vessels; proliferation of these cells had given rise to a tumor.

Resection.—Scholl¹⁹ reported a case in which both kidneys were diseased. The patient, a woman, had symptoms of severe urinary infection. Cystoscopy and the roentgen ray revealed much reduction in function and infection in both kidneys with a large stone in the left kidney.

18. Speciale, F.: Sui periteliomi del rene: Contributo clinico ed anatomopatologico, *Riforma med.* 44:848, 1928.

19. Scholl, A. J.: Kidney Resection, *Ann. Surg.* 88:1045, 1928.

The left kidney was exposed under gas and oxygen anesthesia, through a posterolateral incision; it was almost twice normal size. The lower pole was rounded, bulbous and edematous, and there were extensive inflammatory perirenal adhesions. After the adhesions were stripped off, the lower segment of the kidney was about 6 cm. wide; it felt hardened, but was readily compressible and somewhat fluctuant. The fatty covering over the pelvis was removed, and an incision 2 cm. long was made in the renal pelvis parallel to the long axis of the kidney; this readily exposed the main segment of the calculus, which was removed through this incision. The middle section of the stone projected through the lower calix, where a smaller, rounded mass completely blocked drainage from the lower part of the pelvis. Since it was not possible to remove the stone in one piece, it was broken and the larger fragment was removed through the incision in the pelvis; the other fragment slipped back into the lower part of the kidney. When the lower end of the calculus slipped away from the calix, thick green pus oozed through the opening, indicating that there was pus under pressure in the lower renal segment and that it was confined there by the ball-valve action of the stone. A transverse incision was made in the parenchyma of the kidney in an area in which apparently normal tissue adjoined the swollen lower segment. The incision opened into the abscess cavity, which contained about 90 cc. of thick, green pus. The wall of the cavity, which comprised the entire lower third of the kidney, was thin and fibrous, and contained little functioning tissue. The lower segment of the kidney, which contained several fragments of stone, was resected. The incision in the kidney was sutured with catgut.

Nine months after operation a divided intravenous phenolsulphonphthalein test revealed normal and equal function in both kidneys. Sixteen months after operation the urine from the bladder was not abnormal, and the patient had gained 16 pounds (7.3 Kg.) and was feeling well.

[COMPILERS' NOTE.—This article, with the deductions to be drawn from its conclusions, is in accord with the more recent trend of thought in conservative renal surgery. If the surgeon can maintain good blood supply and proper drainage to the remaining segment, partial nephrectomy probably will give all that may be desired and often will be the means not only of saving the life of the patient but of restoring him to relatively good health. The maintenance of proper drainage, especially during the first few months after operation, is important. With subsidence of the early inflammatory reaction, the drainage of the kidney will be taken care of by the natural route. The value of persistence with the indwelling catheter and of repeated renal lavage, during the period of healing, cannot be overemphasized, and should be

continued even if, from the clinical standpoint, it seems inevitable that the remaining segment must be sacrificed.

Unquestionably, partial nephrectomy will prove to be a new and fruitful resource to the urologic surgeon in many cases that otherwise would be unsatisfactory surgical risks.]

Stone.—Cifuentes²⁰ discussed recurrent renal calculi. In an earlier paper he reviewed 359 cases of pelviolithotomy from the literature in which there was recurrence in 3.9 per cent. He divided the infected from the noninfected cases and found that recurrence occurred in only 1.7 per cent of 226 noninfected cases. In the infected cases there was a recurrence of 7.5 per cent. In 9.5 per cent of 941 cases of nephrotomy there was recurrence. Rovsing reported a high percentage of recurrences, fifty-seven in fifty-one cases. He attributed the recurrence to infection with the staphylococcus and *Bacillus proteus*. Gottstein reported on his own cases in which there was 10 per cent recurrence in aseptic cases and 21 per cent in infected cases.

Retention, as well as infection, favors recurrence. Retention may be secondary to ureteral strictures or kinks. The size of the stone apparently has little influence on recurrence, but it has been observed that phosphatic stones are most prone to recur. Cifuentes advised lavage of the renal pelvis after operation as prophylaxis against recurrence.

[COMPILERS' NOTE.—In discussing recurrence in any series of cases of calculi, many factors of importance may be overlooked and the conclusions which are drawn may be misleading. The chemical composition of the stone, the degree and type of infection present, and the persistence of stasis in the urinary tract from which calculi have been removed are features which should be evaluated in each case but are frequently passed over when a large series of cases is studied as a whole.

In general the incidence of recurrence has been greatly decreased since the advent of roentgenograms at the operating table to avoid leaving small stones or fragments. At the present time, this incidence usually should be less than 10 per cent.

Most urologists state the belief that careful and complete operative removal of stones followed by frequent cystoscopic lavage and such surgical measures as will insure good drainage of the urinary tract are the essential factors in clearing up residual infection and avoiding stasis. From a practical standpoint, infection and stasis sum up what is known as the chief causative agents in the formation of stone. Nevertheless, one must not forget that oxalate stones have been produced experimentally in animals by overloading the calcium oxalate

20. Cifuentes, Pedro: Sur la récidence des calculs du rein, J. d'urol. méd. et chir. 26:289, 1928.

content of the urine, and that such a mechanism may account for recurrent calculi of the oxalate or urate variety, when infection, possibly, is in abeyance.]

Carbuncle.—Lazarus²¹ reported two cases of carbuncle of the kidney. The symptoms are usually pain and tenderness in the lumbar region, accompanied by fever and practically negative urinary data. It is frequently preceded by a carbuncle or furuncle elsewhere in the body. Cystoscopic examination is usually negative.

The treatment is early operative intervention. Simple incision and drainage or excision often cure the disease, and nephrectomy should be performed secondarily only if drainage or excision is not successful. In all cases of perinephritic abscess the kidneys should be explored carefully, since many of these are secondary to carbuncle of the kidney. The lesion usually is produced by an organism of attenuated virulence.

Cystic Disease.—Meltzer²² sent a questionnaire to members of the American Urological Association and compiled reports on 111 cases of polycystic disease of the kidney with surgical symptoms. Nephrectomy was done in fifty-nine cases (53.1 per cent); Rovsing's puncture of cysts was done in thirty-one cases (28 per cent); and decapsulation and puncture were done in five cases. Of the patients treated surgically, four lived forty-eight hours, twenty-four lived from three days to six months, twenty lived from six months to two years, forty-four lived for from two to eight years, three lived nine years, one lived eleven years, one lived twelve years, one lived thirteen years, two lived fourteen years and one lived fifteen years. American urologic experience with this disease reveals that life can be prolonged in 57.6 per cent of the cases for from six months to eight years; in 21.6 per cent, life was maintained from three days to six months after operation.

Clinically, there are apparently no authentic cases of unilateral polycystic disease. If cases supposed to be unilateral in which nephrectomy has been done are traced, evidence of the disease in the supposedly normal and remaining kidney will be found. That unilateral polycystic kidney exists is substantiated by numerous postmortem observations. Preitz found sixteen cases in 1,000 necropsies, and Naumann reported sixteen cases in 10,177 necropsies.

The most commonly accepted explanation of polycystic disease is that it may originate in consequence of embryonic malformations; it is believed also that the condition is both congenital and hereditary.

21. Lazarus, J. A.: Carbuncle of the Kidney: Report of Two Cases. *J. Urol.* **21**:353, 1929.

22. Meltzer, Maurice: A Contribution to the Surgical Aspects of Polycystic Disease of the Kidney. *Brit. J. Urol.* **1**:54, 1929.

Osler reported five cases of polycystic disease in five children of one mother. Crawford mentioned numerous cases of this disease in four generations of one family.

Two significant symptoms which require surgical treatment are brisk and recurrent hematuria or abdominal pain. The pain is colicky either when the ureter becomes obstructed by the passage of pieces of blood clot or débris, or when the renal pelvis becomes distended by such occlusions. Dull abdominal pain is due to distention of the renal pelvis, or to pressure on the abdominal viscera by the enlarged renal tumor. Kidd classified the symptoms in three stages: (1) the stage of progressive enlargement of one or both kidneys without other symptoms; this may last for a few months to several years and may be discovered in the course of abdominal palpation; (2) the stage of renal tumor, in which there may not be pain, but a dull ache in the loin, or local pain and tenderness, and (3) the stage of uremia. The greatest aid to diagnosis, besides the symptoms, is the pyelogram which demonstrates the spindle-like outline of the renal pelvis and calices.

Before surgical treatment is considered, a careful general examination should be made, particularly the estimation of the function of the remaining kidney.

[COMPILERS' NOTE.—Although our knowledge of the genesis of polycystic kidney is somewhat obscure, it does seem that the development of this anomaly is in some way related to perverted union of the collecting and secretory parts of the urinary tract. The condition does not manifest itself until somewhat late in adult life, if we assume an anomaly which exists as the result of embryologic maldevelopment. From the number of cases of unilateral disease noted in postmortem studies, it is likewise remarkable that the condition has not at some time been determined clinically on one side only.]

As Meltzer emphasized, the best operative effort is the control of bleeding and abdominal pain, which places so many of these unfortunate patients in the invalid class. In spite of both sides being diseased, it is noteworthy that American urologists, according to this report, have employed nephrectomy so frequently (in 53.1 per cent of cases). Although such radical treatment may be indicated to give the patient an interval of freedom from pain or bleeding, provided the major symptoms are on the treated side, the ominous prognosis so far as the ultimate fate of the remaining kidney is concerned would lead to the belief that operative procedures should usually be of a type which would preserve as much of the secreting renal epithelium as possible. One would presume that the operation of puncture of cysts, alone or combined with decapsulation, would be the more frequent procedure, even if the function of the opposite kidney was relatively good.]

Meltzer²³ described a case of echinococcus disease of the kidney in which, at operation, the kidney was found to be a pouch about 30 by 20 cm. in size, filled with echinococcus cysts varying from 1 cm. in diameter to 3 by 5 cm. There were approximately from 800 to 900 cysts; about 200 of these came out crushed and macerated.

Twenty-two cases of echinococcus disease of the kidney have been reported. Two cases were also noted at necropsy. Infection of the kidney with echinococcus is rare, because the larva has to go through the liver, heart and lungs and back to and out of the heart before it is started in the systemic circulation for the kidney. The disease is almost always unilateral. The parasite has been known to survive for twenty years. It may be quiescent for years. Renal or ureteral pain is due to the passage of pieces of the wall of a cyst or pieces of blood clot after the rupture of a cyst, frequently causing intermittent ureteral obstruction. Hematuria may also occur with rupture of a cyst.

A diagnosis can be made only by finding the hooklets in the urine after the rupture of a cyst. Associated with the hooklets are pus cells and erythrocytes depending on the degree of infection. If the process is of long standing, a definite tumor of the kidney may be palpated. Eosinophilia is reported in more than half of the cases.

Nephrectomy is indicated as soon as the diagnosis is made. Of sixteen patients on whom nephrectomy was performed for hydatid disease of the kidney, ten are said to be cured and three improved. Foreign surgeons prefer conservative measures, such as incision and drainage and marsupialization.

Hydronephrosis.—Morison²⁴ attempted to determine the routes of absorption in hydronephrosis by introducing dyes into the renal pelvis in amounts less than the total pelvic capacity. He observed two routes of absorption, lymphatic and tubular. At the beginning of complete ureteral obstruction there is, for the first two or three days, lymphatic absorption from the walls of the renal pelvis and ureter. Tubular absorption begins after about the third day and continues more actively than lymphatic absorption. A short period of backpressure favors tubular absorption. The convoluted tubules of the peripheral glomeruli are the first to take on this function; as atrophy from pressure progressively supervenes, the subjacent layers continue the progress of reabsorption. In absorbing dye, the cells of the convoluted tubules may demonstrate a slightly altered function. If so, their action would tend to favor the filtration and reabsorption theory of renal secretion.

23. Meltzer, Maurice: Echinococcus Cysts of the Kidney, *J. A. M. A.* **92**:1925 (June 8) 1929.

24. Morison, D. M.: Routes of Absorption in Hydronephrosis; Experimentation with Dyes in the Totally Obstructed Ureter, *Brit. J. Urol.* **1**:30, 1929.

Morison stated the belief that pyelovenous backflow is probably the result of trauma and cannot be regarded as a usual factor in the mechanism of hydronephrosis.

[COMPILERS' NOTE.—The concept of pyelovenous backflow as introduced by Hinman several years ago has been the subject of sharp debate. Morison's experiments and his conclusions obviously place him in the ranks of those opposed to this concept. Whether a relatively open system of communication, physiologic in type, between the venous system and the collecting tubules and pelvis, exists normally is difficult to demonstrate to the satisfaction of all interested in urologic physiology. It is noteworthy that Morison filled the pelvis in amounts less than the pelvic capacity. To what degree the pelvis is to be filled in order to initiate pyelovenous absorption without the actual occurrence of traumatic rupture of the venules is the chief point which is to be determined experimentally. Pressure relationships in the renal pelvis in both normal and hydronephrotic states are elusive in actual determination. It will be interesting to note the advance of knowledge along this line within the next few years.]

Perinephritis.—Larru²⁵ discussed the roentgenologic diagnosis of nonpurulent perinephritis. He noted the disappearance of the outer border of the psoas muscle in its upper part and also the entire or partial disappearance of the inner border of the renal shadow. The two shadows appear to be superimposed on one another. The explanation is that perinephritis, especially inflammation of the psoas muscle, is present, which tends to destroy the outline. It may be found in all renal conditions that tend to cause perirenal adhesions, especially to the psoas muscle, such as calculous pyonephrosis, perinephritic abscess, or renal tuberculosis. Larru found it constantly in renal tuberculosis.

Technic for Removal.—Cathelin²⁶ divided the types of diseased kidneys which should not be removed into several categories: 1. The adherent pyonephrotic calculous type, especially with adhesions at the level of the hilum, should not be removed because a cleavage plane does not result from the multiple adhesions to surrounding structures. On the other hand, the subcapsular operation exposes only the firm sclerosed hilum, which cannot be accurately ligated. Cathelin stated the belief that the most logical procedure in these cases is simple nephrostomy with digital extraction of the stones. 2. Nephrectomy should not be performed in cases in which a tuberculous kidney is apparently normal. If, during the course of an exploratory operation, the kidney and ureter

25. Larru, E.: Roentgendiagnose der Perinephritis, An. de acad. med.-quirug. espanola 14:236, 1928.

26. Cathelin: Les reins qu'il ne faut pas enlever, J. d. praticiens, 1929, p. 17.

appear normal, it is better to leave the kidney in place, even if it might necessitate operation later following recurrence or aggravation of the symptoms. 3 A large, adherent carcinomatous kidney should not be removed in young or old patients. In middle-aged patients nephrectomy is indicated in such cases. 4 Removal of a sclerosed kidney, after an old perinephritic abscess has been opened, would not result satisfactorily and the patient, already weakened, would have to be under anesthesia too long. 5 Nephrectomy should not be done in the presence of a deep atrophied renal mass and extensive sclerolipomatosis.

SUPRARENAL GLANDS

Technic for Removal—Stultz and Stricker¹ reported a series of cases of epinephrectomy, a surgical procedure which in some instances comes within the province of urology.

They described the following technic. The patient is placed as for left nephrectomy, on a lumbar support which can be raised at will. The right leg is kept flexed, and the left leg is stretched, the plane supporting the lower limbs is inclined, so that the ilio-costal space is widened as much as possible. A lateral incision is made from 12 to 15 cm. long, beginning one or two fingerwidths from the outer border of the left rectus abdominus muscle, slightly above or at the level of the umbilicus. It runs toward the upper margin of the twelfth rib, strikes it under an acute angle, crosses the rib and ends near the external border of the erector spinae muscles. The twelfth rib is resected for a length of from 5 to 8 cm. When the kidney has been identified, the fatty capsule is opened by an incision near the inner border of the upper pole of the kidney and is freed from the perirenal fat. With a large retractor the kidney is pushed downward and forward in the direction of the pubis, so as to facilitate exposure of the subphrenic space. This manipulation also drags down the suprarenal gland, which is still wrapped in its fat, by means of the vascular pedicles that branch from the renal vessels. The gland is then searched for in the epirenal fat, and its base, which faces downward, backward and outward, is usually discovered first. The suprarenal tissue is recognized by its yellow tint and is easily distinguished from fat. The gland is sectioned above a ligature, with the knife directed toward the kidney. A part of the glandular tissue is left behind because of the possibility that the opposite suprarenal gland may be absent or deficient.

In thirteen cases epinephrectomy did not injure the pleura. During operation on a cadaver the pleura was injured because the incision was made too high and too far posteriorly, between the eleventh and twelfth

¹ 27 Stultz, E., and Stricker, P. Technique of Left Epinephrectomy. Surg Gynec Obst 48:487 1929.

ribs. The peritoneum is not injured if care is taken to split the fatty capsule of the kidney far behind. The postoperative course is usually normal. The patients have practically no fever, never suffer from shock, and their recovery is rapid.

URETER

Anomalies—Spitzer and Wallin²⁸ presented a case in which both kidneys were normal, each containing one normal pelvis and each pelvis leading to the bladder by a ureter which was normally placed. There were also two accessory bodies, one resting above each kidney, which secreted a fluid in no way resembling urine. This fluid was conducted outside the body by tubes which opened at the position of the para-urethral ducts, one on each side of the median line. These tubes followed the course in the walls of the bladder and vagina that is usually taken by Gartner's canal, known to be the persistent remains of the mesonephric duct.

Spitzer and Wallin attempted to classify the so-called ectopic ureters so as to distinguish those that are supernumerary from those that are not.

Infection of Stump—O'Neil²⁹ reported a case in which he performed nephrectomy for congenital dilatation of the renal pelvis and the ureter. He removed a portion of the ureter. Cloudy urine later developed. At cystoscopic examination, the stump of the ureter was washed out and a ureterogram showed a sausage-shaped shadow several centimeters long. Dilatation of the orifice of the ureter, proper drainage, and one or two irrigations with silver nitrate effected a complete cure. The author expressed the belief that, in cases of congenital dilatation of the ureter necessitating nephrectomy, complete ureterectomy is indicated.

Wildbolz³⁰ observed that ureteritis which develops after nephrectomy usually heals spontaneously or after the ureter has been lavaged a few times. As a rule it occurs during the first six months after nephrectomy. He reported a case of a woman, aged 30 years, in whom infection of the ureteral stump occurred unusually late after nephrectomy for nontuberculous pyonephrosis. A year after nephrectomy she went through pregnancy without any complications. Three years after operation, during another pregnancy, she did not feel well and ran a high continuous fever, the urine became purulent. After normal delivery, the fever continued. Renal tests showed good renal function.

²⁸ Spitzer W. M. and Wallin I. E. Supernumerary Ectopic Ureters. *Ann Surg* **88**:1053, 1928.

²⁹ O'Neil R. F. Discussion. *J Urol* **21**:119, 1929.

³⁰ Wildbolz Hans. Discussion, *J Urol* **21**:122, 1929.

in spite of the enormous quantity of pus in the urine. Catheterization of the only kidney revealed clear urine. The pus came from the ureteral stump of the side on which the kidney had been removed. The patient refused surgical intervention. Recovery was complete after treatment by lavage of the ureteral stump.

Stones.—Bumpus³¹ reported 1,001 cases in which the diagnosis was stone in the ureter in a clinical study covering a period of nine years. Pain originating in the renal area and radiating toward the bladder was noted in 634 cases (63.4 per cent). Pain in the lower right quadrant without radiation and with little suggestion of renal colic occurred in 138 cases. Removal of the appendix, without relief from symptoms, had been done in thirty-seven of the 138 cases, an incidence of 26.8 per cent. In 226 cases the appendix had been removed.

In 146 cases the stone passed following the manipulation during the first cystoscopic examination, and in 274 other cases manipulation was followed by success in 202 cases. Manipulation was successful in 74 per cent of the cases in which it was attempted, with the exclusion of the 146 cases in which stones passed after a single cystoscopic examination with inclusion of these 146 cases. Manipulation was successful in 85 per cent in which it was attempted.

There were 252 cases of stone in the lower third of the ureter removed surgically and 228 in the upper and middle thirds. In forty-nine cases the urinary obstruction produced by the stone had resulted in such extreme ureteral and renal injury that nephrectomy or nephroureterectomy was required. Except in these forty-nine cases, 60 per cent of all the stones in the lower part of the ureter were removed by manipulation. Reactions occurred thirty-two times (11 per cent) in 274 cases in which manipulation was carried out; two fatal cases were included in this number, in both of which surgical intervention was refused for several days after the suppurative nephritis incident to the manipulation had occurred. Bumpus stated the belief that patients in whom there is marked infection, as well as patients with stones of more than from 1.5 to 2 cm. in diameter that are known to have been present for a considerable period, should be treated by ureterolithotomy rather than by manipulation. Reaction following manipulation can be reduced to the minimum if ureteral catheters are left in the ureter to insure drainage after the stone has been removed. In all the cases in which operation was performed as soon as signs of renal infection appeared, the patients recovered, whereas in the two cases in which it was delayed the patients died. The mortality after catheter manipulation for the entire series was 0.2 per cent.

31. Bumpus, H. C.: A Clinical Study of Stones in the Ureter, *Proc. Staff Meet. Mayo Clinic* 4:140, 1929.

Stricture.—Braasch³² stated that the only visual evidence of ureteral obstruction is caused by dilatation which persists in repeated ureterograms. That ureteral dilatation occurs early is evident from the dilatation which is always found in the presence of ureteral stones, even if they are small or if they have been present in the ureter only a short time. A factor which may confuse the interpretation of stricture is the dilatation occurring in the ureteral wall as the result of inflammatory changes or atony. The deformity of the ureter may vary from scarcely recognizable irregularity to marked dilatation. Ureteral dilatation as the result of obstruction is usually greater than that which accompanies inflammation. If the dilatation of the ureter results largely from obstruction, it assumes a more uniform outline, particularly if there are single areas of obstruction such as occur in cases of ureteral stone.

Extra-ureteral factors may also be the cause of ureteral obstruction, particularly in the female pelvis, where either inflammatory or malignant tumors which involve the pelvic organs may also involve the ureter. Spasm of the ureteral wall is another probable cause of localized ureteral constriction. Evidence of spasmodic constriction at or near the ureteropelvic juncture, with stone in the renal pelvis, is frequently observed. It usually occurs only in the presence of a single, comparatively small stone, situated in the true renal pelvis, and is probably the result of local irritation. Spasmodic constriction of the ureter is occasionally observed in hypersensitive patients as the result of irritation from the ureteral catheter.

The diagnosis of ureteral stricture by means of the urogram may be difficult. Unless the changes in the wall of the ureter are considerable and definite, it is questionable whether a conclusive diagnosis of ureteral dilatation can be made.

Obstruction.—Hyams³³ stated that obstruction of the lower or pelvic portion of the ureter may be produced by blood vessels which may be normal to the region but pursue an atypical course, or by structures foreign to the area through which they run. The possibility of obstruction should be borne in mind both before and at the time of operation. Treatment is operative in a large percentage of cases. He stated the belief that the subject is of sufficient importance to warrant careful investigation and future anatomic and clinical research.

[COMPILERS' NOTE.—Obstruction in the upper part of the urinary tract produced by aberrant blood vessels is well known and is frequently

32. Braasch, W. F.: Roentgenologic Diagnosis of Ureteral Stricture, *Radiology* 12:183, 1929.

33. Hyams, J. A.: Aberrant Blood Vessels as a Factor in Lower Ureteral Obstruction, *Surg. Gynec. Obst.* 48:474, 1929.

treated by surgical procedures. Obstruction in the lower part of the tract may be caused by pressure changes at the point of crossing of the vas deferens in the male or of the uterine arteries in the female. However, the occurrence of anomalous blood vessels crossing the pelvic ureter and producing varying degrees of obstruction has not been given much anatomic or clinical consideration. The report of Hyams, especially of his observations at necropsy, is illuminating, and should be the stimulus for much careful investigation along this line. Unquestionably there is reason to assume that a many-branched vessel, like the hypogastric, would be the seat of variations from time to time, as are many-branched vessels in other parts of the body, for example, the renal and hepatic arteries. Hyams seems to have demonstrated definitely that such abnormal branches can compress the ureter in its pelvic portion.]

Marion³¹ reported the case of a man, aged 27 years, who gave the following history: At the age of 3 years he had some difficulty in urination. Operation for phimosis did not improve the condition. At the age of 4 he had an attack of hematuria which lasted two days. Since childhood he had had intermittent incontinence, especially at night. At the age of 20, he had had severe hematuria after riding horseback. A large stone was found in the bladder and was removed, but even this did not completely relieve the symptoms. Intravesical cystic dilatation of the left ureter was later found at cystoscopic examination. The urine of the right side was normal; that of the left was thick and purulent. Left nephrectomy was performed and the symptoms disappeared. Apparently the incontinence was not the result of stone, which had existed since childhood, but of infection and distention of the left kidney. Marion stated the belief that this case was somewhat analogous to the occasional occurrence of periods of incontinence in cases of renal tuberculosis.

34. Marion: Dilatation kystique intravésicale de l'extrémité inférieure de l'uretère et lithiase vésicale infantile infectée; incontinence infantile guérie par disparition de la dilatation kystique, *Soc. Française d'urolog.*, Séance de 17 décembre 28, *Presse méd.* 7:112, 1929.

(To be Continued)

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VALUE OF BLOOD AMYLASE ESTIMATIONS IN THE DIAGNOSIS OF PANCREATIC DISEASE

A CLINICAL STUDY *

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The clinical diagnosis of disease of the pancreas¹ has always been fraught with great difficulty. Whether one is dealing with the dramatic suddenness of an acute hemorrhagic pancreatitis, the silent jaundice in carcinoma at the head of the pancreas, the variable and indefinite symptomatology of chronic pancreatitis or the insidiously developing pancreatic cyst, a large proportion of pancreatic lesions remain unrecognized clinically and are first diagnosed at laparotomy or at postmortem examination. This is not because the pancreas is so rarely the seat of disease, for it is diseased far more frequently than is generally supposed. Among the 60,000 patients admitted to Barnes Hospital but 150, or 0.25 per cent of the cases, bore a diagnosis of pancreatic disease of one kind or another, exclusive of diabetes mellitus, while among the last 3,600 autopsies performed at the Washington University School of Medicine, gross or microscopic lesions of the acinar tissue were found in 113, or in 3 per cent of the cases. This is in substantial agreement with the observations of others.² On the other hand, a more frequent incidence is reported by Moench,³ who found acute pancreatitis alone in 2 per cent of routine autopsies.

Many efforts have been made to test the function of the pancreas in the attempt to recognize disease of it clinically. Tests of kidney and of liver function have been so fruitful of results that a similar usefulness seemed possible in the case of the pancreas. The literature concerning

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1. Only disease of the external secretion is here considered. Glycosuria as a sign of lesion in the islets, when noted, was secondary to disease of the acini and ducts.

2. Barron, M.: Disease of Pancreas, Pathologic Study, with Report of Cases, Arch. Int. Med. 35:807 (June) 1925.

3. Moench, G. L.: Acute Pancreatitis with Erosion of Splenic Artery and Fatal Hemorrhage, J. A. M. A. 82:360 (Feb. 2) 1924.

these attempts is extensive. In a recent monograph on pancreatic disease,⁴ fourteen different tests for pancreatic function were described; several more exist which were not mentioned. The majority of them, however, have fallen into desuetude and at present have only a historical interest.

In this paper, consideration will be confined to the amylase content of the blood serum, since this starch-splitting ferment is one of the prominent enzymes elaborated by the pancreas, and because it lends itself readily to quantitative measurement. Moreover, many observers have studied it in the attempt to correlate deviations from the normal with the existence of pancreatic disease. The methods used have been various, and the great variability in the observations may be ascribed, in part at least, to this circumstance.

PREVIOUS OBSERVATIONS

A starch-splitting ferment, diastase, or more accurately, amylase, was first found in the blood by Magendie in 1846. Although diastase was extensively studied as it occurred in the vegetable kingdom, the first attempt to measure it quantitatively in the animal organism was made by Foster⁵ in 1867. Among other things, he found that in the blood from six diabetic patients there was no deviation from the diastatic activity of normal blood. The details of his quantitative method were not recorded.

The nature of the various sources of amylase occurring in the animal organism next attracted the attention of physiologists. From the work of a series of observers, summarized by Carlson and Luckhardt⁶ in 1908, it was established that the amylase in the blood had the same properties as that present in the lymph, saliva, liver and pancreas; that is, it had the power to break down starch to the dextrins and finally to dextrose. The concentration of the ferment was found to be greatest in the pancreas and least in the cerebrospinal fluid.

The origin of the amylase found in the blood is of special interest and has been the object of much work and some difference of opinion. Carlson and Luckhardt⁶ believed, on the basis of their own observations, that it was merely a by-product of general tissue metabolism. They found no change in blood amylase in three cats following pancreatectomy, an observation confirmed by Bainbridge and Beddard⁷ in one cat, and by Milne and Peters⁸ in several dogs. Many workers found greater amounts in the blood leaving than in that entering the

4. Gross, O., and Guleke, N.: *Die Erkrankungen des Pankreas*, Berlin, Julius Springer, 1924, p. 39.

5. Foster, M.: *J. Anat. & Physiol.* **1**:107, 1867.

6. Carlson, A. J., and Luckhardt, A. B.: *Am. J. Physiol.* **23**:148, 1908.

7. Bainbridge, F. A., and Beddard, A. P.: *Biochem. J.* **2**:89, 1907.

8. Milne, L. S., and Peters, H. L.: *J. M. Research* **26**:415, 1912.

liver, and concluded that the liver manufactures the ferment. Carlson and Luckhardt,⁶ on the contrary, found no difference in amylase concentration in blood from the hepatic artery and vein. Davis and Ross⁹ adduced further evidence that the liver did not manufacture diastase. When they administered toxic amounts of chloroform to dogs, a marked decrease in blood amylase was found, but since no change occurred in depancreatized dogs, they concluded that the decrease in the first experiments was due to toxic changes in the pancreas rather than in the liver.

The pancreatic origin of blood amylase was first promulgated by Schlesinger,¹⁰ who found in two dogs and one cat a diminution or a disappearance of the enzyme in the blood after pancreatectomy. King¹¹ found a uniform decrease or disappearance of urinary amylase and a decrease in the blood from one half to one third of the normal level in four dogs and two cats after pancreatectomy. Wohlgemuth,¹² Moeckel and Rost,¹³ Lepine,¹⁴ Kaufmann,¹⁵ Gould and Carlson,¹⁶ Otten and Galloway,¹⁷ and Davis and Ross⁹ have all had similar results. Moreover, Schlesinger found from three to four times as much ferment in blood leaving the pancreas as in the general circulation, an observation confirmed by Wohlgemuth. King, as further evidence of the pancreatic origin of at least part of the blood amylase, showed that the amount of the ferment in puppies and kittens increased from a low level at birth to the normal adult value at 6 weeks of age. This fits in with the observations of Korowin,¹⁸ who found no amylase in the human pancreas at birth and an increasing amount after the second month up to 1 year of age, when it reached the normal adult concentration. That the salivary gland does not contribute to the presence of blood amylase is indicated by his observation that its content of diastase is large and remains the same from birth on. Schlesinger,¹⁰ moreover, in extirpations of the salivary glands in dogs, found no significant change in the blood. The observations of King,¹¹ published in 1914, and also those of Davis and Ross⁹ are probably of greater value than those of others because they used a more accurate quantitative method. Amylase was measured by the time required to effect a given change in the starch solution rather

9. Davis, L. H., and Ross, E. L.: *Am. J. Physiol.* **56**:22, 1921.

10. Schlesinger, W.: *Verhandl. d. Kong. f. inn. Med.* **25**:505, 1908; *Deutsche med. Wchnschr.* **34**:593, 1908.

11. King, C. E.: *Am. J. Physiol.* **35**:301, 1914.

12. Wohlgemuth, J.: *Verhandl. d. Kong. f. inn. Med.* **25**:501, 1908.

13. Moeckel, K., and Rost, F.: *Ztschr. f. physiol. Chem.* **67**:433, 1910.

14. Lepine, R., and Barral, M.: *Compt. rend. Acad. d. sc.* **113**:729, 1891.

15. Kaufmann, M.: *Compt. rend. Soc. de biol.* **46**:130, 1894.

16. Gould, L. K., and Carlson, A. J.: *Am. J. Physiol.* **29**:165, 1912.

17. Otten, H., and Galloway, T. C., Jr.: *Am. J. Physiol.* **26**:347, 1910.

18. Korowin: *Malys Jahresb.* **3**:158, 1873.

than by the amount of change effected in a given time, following thus the technic of Roberts,¹⁹ reported in 1881, and more recently shown by Bayliss²⁰ to be the most reliable principle in measuring such a ferment as amylase.

The evidence thus far seems to point to the pancreatic origin, in part at least, of blood amylase and to lend a theoretical basis to attempts to correlate deviations from the normal concentration of this enzyme in the blood with the existence of pancreatic disease. Other experimental facts add further support to this association.

Ligation of the pancreatic ducts in animals leads to a prompt increase in the concentration of blood amylase, as shown in an experiment performed by Schlesinger,¹⁰ Clerc and Loeper,²¹ King,¹¹ Wohlgemuth,¹² Gould and Carlson¹⁶ and others with uniform results. King¹¹ noted a return to normal in about a week, but at autopsy found that the ligatures had slipped and that the ducts were functioning again. In unpublished data from this laboratory we have demonstrated a fourfold increase in blood amylase within fifteen minutes after clamping of the tube that drained all of the pancreatic juice in dogs. This increase rose to a point seventy-five times greater than the normal in twenty-four hours, after which the concentration gradually fell to normal in two weeks. No dogs were observed after this length of time. Autopsy showed a hard, enlarged pancreas with beginning atrophy of the acini. It is difficult to keep a dog alive longer than this after careful and complete obstruction of the ducts. We did not, therefore, study the blood amylase at a time when the acini were fully atrophied.

The clinical investigation of blood amylase has been rather extensive. One of the most widely used methods is that of Wohlgemuth²² which depends for its end-point on the complete hydrolysis of starch as revealed by the disappearance of the blue color which it produces with iodine. In thirty normal persons, Wohlgemuth¹² himself found "considerable fluctuation" (no numerical values being reported). In twenty patients with a variety of conditions Schlesinger¹⁰ found variations expressed by numerical values between 10 and 25. In fifty cases, Von Benczur²³ reported differences too great to be of diagnostic value (from 16 to 250) except in one case of obstruction of the pancreatic duct in which the value was considerably higher than in the others (500). The observations of other workers were more promising. Thus Corbett,²⁴ in 1912,

19. Roberts, W.: *Proc. Roy. Soc. Med.* **32**:145, 1881.

20. Bayliss, W.: *Theory of Enzyme Action*, New York, Longmans Green & Company, 1924, ed. 5, p. 52.

21. Clerc, A., and Loeper, M.: *Compt. rend. Soc. de biol.* **66**:871, 1909.

22. Wohlgemuth, J.: *Biochem. Ztschr.* **9**:1, 1908.

23. Von Benczur, J.: *Wien. med. Wchnschr.* **23**:890, 1910.

24. Corbett, D.: *Quart. J. Med.* **6**:351, 1912.

found that the values were constant in normal persons and that the value of blood amylase was unchanged by diet. Stafford and Addis²⁵ and Cohen²⁶ and Stocks²⁷ similarly reported a uniformity in the concentration of "normal" human blood amylase.

An alternative method for determining blood amylase has been used by many. It depends, not on the disappearance of starch, but on the formation of sugar which is measured quantitatively by some method of copper reduction. Kaufmann,¹⁵ and Moeckel and Rost¹³ were the earliest to use this method on blood serum. The latter workers found that feeding had no influence on the value of blood amylase, that a prolonged fast resulted in some increase, and that although different species varied considerably, individuals among the same species differed little from each other, observations which were in general agreement with the work of others. Reid²⁸ reported uniform values for human beings, varying between numerical values of 6 and 10, Meyer and Killian²⁹ values between 15 and 17, and Lewis and Mason³⁰ between 15 and 25, all using the sugar reduction method.

Definite deviations from the normal in pancreatic disease have been reported by many writers. Stocks²⁷ studied sixty-five cases and found an increased blood amylase in carcinoma of the pancreas, nephritis and chronic passive congestion, and in three of eight cases of diabetes. Meyer and Killian²⁹ recorded an increase from the normal value 15 to values from 41 to 75 in diabetes and to values from 30 to 52 in nephritis, the latter varying in general with the degree of retention of nitrogen. Lewis and Mason,³⁰ however, following the same technic, failed to confirm these observations in cases of diabetes; while variations were noted in nephritis, there was no correlation with the type of disease or with its progress.

The lack of uniformity in the clinical observations briefly summarized is probably due to several factors. Discrepancies in the methods used have undoubtedly a good deal to do with many of the differences. In the beginning of our studies on blood amylase, we tried the starch-iodine as well as the sugar reduction method, and found both unsatisfactory for reasons already mentioned.³¹ The method finally adopted applied a new principle to the study of amylase, and it is one which, we believe, has yielded more consistent results. Another factor in the results of

25. Stafford, D. D., and Addis, T.: *Quart. J. Med.* **17**:151, 1924.

26. Cohen, I.: *Brit. J. Exper. Path.* **6**:173, 1925.

27. Stocks, P.: *Quart. J. Med.* **9**:216, 1916.

28. Reid, C.: *Brit. J. Exper. Path.* **6**:314, 1925.

29. Meyer, V. C., and Killian, J. A.: *J. Biol. Chem.* **29**:179, 1917.

30. Lewis, D. S., and Mason, E. H.: *J. Biol. Chem.* **44**:455, 1920.

31. Elman, R., and McCaughan, J. M.: Quantitative Determination of Blood Amylase with Viscosimeter, *Arch. Int. Med.* **40**:58 (July) 1927.

other writers is the fact that in but few instances was the clinical diagnosis confirmed by operation or autopsy. In the series of cases here reported, with two exceptions, each diagnosis depended on the observations at laparotomy or on postmortem examination.

EXPERIMENTAL WORK

The determination of amylase was made by a new method which apparently has never been used before for the measurement of the ferment in blood. It is based on the rate of diminution of the viscosity of a starch solution, as described in a previous paper.³¹ The method enables one to follow quantitatively and continuously the course of the diastatic reaction, that is, the breaking down of starch to dextrose, for each step of the reaction involves, of course, the hydrolysis of larger to smaller molecules and hence a reduction of viscosity.

This circumstance has two immediate advantages: First, every step of the diastatic reaction becomes measurable at the same time. In the Wohlgemuth method²² the disappearance of starch is the only step considered, whereas in that of Moeckel and Rost¹³ it is only the final production of sugar that is measured. It is obvious that the enzyme may attack any part or all of the chain and at varying rates. It is thus impossible without extensive work to tell whether all the starch is hydrolyzed first or whether only a part of it is attacked and carried all the way to dextrose. By measuring the viscosity all stages of the reaction become detectable at one time.

The second advantage lies in the fact that one can use time as a measure of enzyme concentration, which is the most accurate correlation since an enzyme acts on the rate of reaction. As pointed out by Bayliss,²⁰ in case of a reaction proceeding in steps, ferment concentration is best estimated by the time required to effect a given change rather than by the amount of change effected in a given period of time. By the method used in this study, it was possible to do this. An arbitrary amount of change was selected (20 per cent reduction in viscosity), and the amount of amylase then became a function of the time required to effect this change.

A final advantage of the present method lies in its objectiveness. The measure of time was made by a stop-watch, and the difficulty of selecting a color change as in the Wohlgemuth method was obviated.

For the use of the method one needs: (1) the set-up for measuring viscosity, that is, the viscosimeters, and (2) the preparation of a solution, or rather a suspension, of starch of constant composition.

Viscosimeter.—The instrument used is of the type originally designed by Ostwald. It is U-shaped with a capillary tube and bulb inserted into one arm (fig. 1). The starch solution (5 cc. of a 3 per cent solution) is introduced into

one arm of the tube and, by suction on a rubber tube, is drawn above the upper mark into the other arm, whereupon the suction is released. As the level of the fluid passes this point the stop-watch is started, and as the second mark just below the bulb is passed the watch is stopped. This time interval (in seconds) is taken as the measure of viscosity. Viscosimeters were selected which had an outflow time for water of from 15 to 20 seconds, or for the starch solution of from 40 to 50 seconds. This short period enables one to make more rapid readings and gives values as accurate as those with tubes having a much longer outflow time. Several readings are made to check the constancy of the viscosity, and

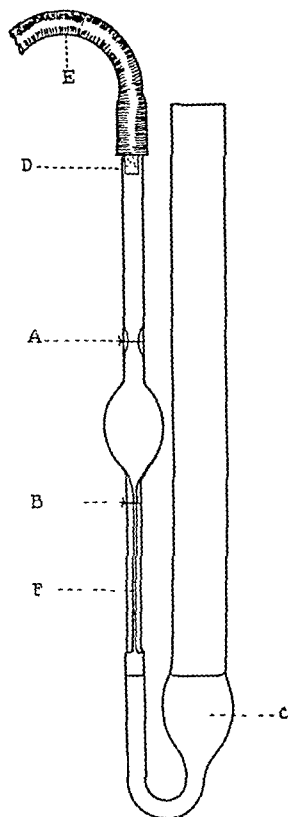


Fig. 1.—The Ostwald viscosimeter. Solution C is introduced into the open end of a glass U-tube. By suction on rubber tube E, it is drawn above point A and the suction is removed. The time of outflow from point A to point B is taken as a measure of the viscosity (in seconds). The resistance is due to the capillary tube F. A plug of cotton D protects the solution from contamination by particles of saliva.

ordinarily 0.4 cc. of the plasma to be tested is added. A few bubbles of air are blown through to insure mixing, and readings are made every few minutes until there is a 20 per cent reduction in the outflow time, that is, in the viscosity. The number of minutes required to reach this point is recorded. A graph may be plotted if desired with viscosity in seconds, and time in minutes, as axes. It

forms almost a logarithmic curve, and, as reported in our previous communication³¹ this time interval, in minutes, bears an inverse linear relation to the amount of amylase added, that is, the reaction follows Arrhenius' rule, $T = \frac{1}{Q}$, where T equals the time required to effect a given change and Q equals the concentration of enzyme used to effect this change. The addition of 0.4 cc. of blood plasma to 5 cc. of starch solution affects the initial viscosity so little that no correction is necessary for the zero point. This is due to the fact that the blood plasma has about the same viscosity as the starch preparation that we used. In the case of plasma with higher concentrations of amylase a smaller amount may be added, that is, 0.1 instead of 0.4 cc.

The set-up is represented in figure 2. A water-bath with glass sides is used, the back wall being frosted. A light behind it gives satisfactory illumination. The water is kept in circulation by air blown through it, and the temperature is maintained at $37.5\text{ C.} \pm 0.1\text{ C.}$ by means of a mercury thermostat and a small gas flame. The viscosimeters, as well as all pipets, are plugged with cotton to preclude the entrance of particles of saliva. All glassware is kept scrupulously clean, for any adhering particle may affect the passage of fluid through the capillary tube. As a routine, the following solutions are run through before being used each time: cleaning solution, tap water, alcohol and ether.

Starch Solution.—We found variations in the composition of various preparations of soluble starch, so that for any series of observations it is necessary to obtain a good supply and to use the same preparation throughout. The batch that we are now using is made up as follows: Three grams are weighed out and added to 70 cc. of cold distilled water and shaken until the suspension is homogeneous. It is then brought to boil over a free flame, with constant shaking, in not less than three minutes, although a longer period does not alter the properties of the final solution. Thirty cubic centimeters of Sørensen's fifteenth-molar phosphate buffer is added ($\text{pH } 6.8$), and the flask is stoppered with a cotton plug and autoclaved for fifteen minutes at 10 pounds' (4.5 Kg.) pressure. Just before it is ready to use it is filtered through paper, and 5 cc. portions are transferred to the viscosimeters. The solution, if kept sterile at 37 C. , may stand for from several hours to a day or two without altering its usefulness, but if kept for several days changes seem to occur. Blood is obtained by venipuncture; it is oxalated, and the clear plasma used. Standing in the icebox for from twelve to twenty-four hours does not alter its diastatic power, but longer periods may do so.

Calculation of Amylase Units.—With 0.4 cc. of normal oxalated plasma from the human adult a reduction of 20 per cent in the outflow time is effected in about thirty minutes, or with 0.2 cc. in sixty minutes. One unit is arbitrarily taken as the amount of enzyme in 1 cc. which will reduce the viscosity 20 per cent in one hour. The formula for determining amylase units (A.U.) on this basis is $\text{A.U.} = \frac{60}{T.V.}$, which is simply Arrhenius' rule with the factor of concentration added. In the foregoing formula, A.U. equals units per cubic centimeter, T time (in minutes) required to reduce the viscosity 20 per cent and V volume of enzyme solution (plasma) used to effect this change.

It was found convenient to have a solution of saliva or of pancreatic juice diluted so that 0.1 cc. of it was as active as 0.4 cc. of normal human serum. It keeps well in the icebox for several months or more, provided a crystal of thymol is added. In this way a standard control was available at all times without the necessity of obtaining normal plasma.

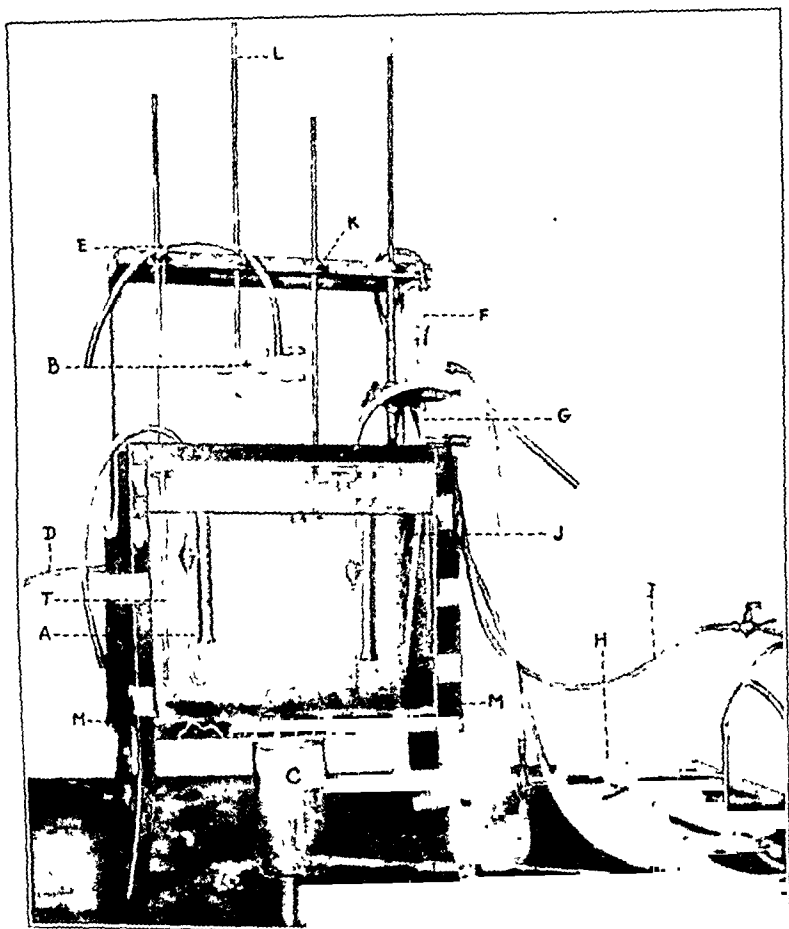


Fig. 2.—Viscosimeter set-up for amylase estimations. The Ostwald viscosimeter *A* is attached to a brass spring clamp *B* which in turn is fastened to the brass rod *L*, movable in the frame and held tight by the screw *K*. In this way the viscosimeter may be lowered into or removed from the water bath. The solution in the viscosimeter is drawn up to the upper mark by suction on the rubber tube *E*. A desk lamp *D* illuminates the bath from behind.

The water bath is kept warm by the gas flame *C* which is automatically regulated through the mercury thermostat *G*. The gas inlet *F* is a tube drawn to a capillary point which is placed just at the level of the mercury when the temperature *T* is at 37.5 C. A by-pass *H* keeps a tiny pilot light always burning. The water bath is insulated on each side by felt pads *M*, and the water is kept in circulation by an inlet of air *I* which bubbles through a glass tube *J*.

OBSERVATIONS

We have prepared tables and clinical abstracts of our observations which are almost self-explanatory. The observations on the blood amylase in a series of twenty-five "normal" controls, not operated on, are presented in table 1. The only criterion of normality so far as the pancreas was concerned was that no suggestion of pancreatic disease was evident in any case. Two patients with diabetes are included in this list since they too gave no indication of disease of the acinar tissue. The blood amylase in all cases was within what we have designated as "normal" limits, that is, from 4.3 to 6.8 units, although most of the cases showed values within a closer range than this. In table 2 are listed data

TABLE 1.—*Amylase Units in the Plasma of a Series of Unselected Patients*

	Case	Date	Age	Sex	Diagnosis	Amylase Units
1	(M. J.)	4/22/27	31	F	Early pregnancy	4.5
2	(J. W.)	4/22/27	58	M	Cataract	5.0
3	(R. S.)	4/23/27	24	M	Hernia	4.5
4	(A. T.)	4/23/27	28	M	Bronchiectasis	5.1
5	(E. H.)	4/23/27	19	M	Tuberculosis of the hip.....	4.7
6	(L. B.)	7/10/27	54	F	Diabetes	6.0
7	(M. E.)	7/16/27	16	F	Deformity of the nose.....	6.1
8	(R. M.)	7/19/27	45	M	Colostomy	5.5
9	(A. B.)	8/ 8/27	30	M	Normal	4.8
10	(J. S.)	9/23/27	38	M	Fracture of the spine.....	6.2
11	(M. L.)	10/27/27	24	F	Dislocation of the neck.....	6.5
12	(M. P.)	11/ 1/27	29	F	Hysteria	5.4
13	(S. S.)	11/ 9/27	61	M	Prostatectomy	6.8
14	(J. H.)	1/23/28	45	M	Sarcoma of the humerus.....	6.5
15	(A. H.)	2/16/28	30	M	Bronchiectasis	4.8
16	(J. D. B.)	2/20/28	60	M	Arteriosclerosis	6.2
17	(E. H.)	2/20/28	30	F	Pernicious anemia	6.0
18	(T. T.)	3/ 5/28	24	M	Hernia	4.3
19	(C. W.)	3/13/28	50	F	Carcinoma of the breast.....	6.2
20	(M. R.)	3/13/28	42	F	Intestinal fistula	5.0
21	(R. T.)	3/25/28	72	F	Pulmonary tuberculosis.....	6.0
22	(A. W.)	10/13/28	42	F	Carcinoma of the breast.....	6.5
23	(A. R.)	10/25/28	68	M	Arteriosclerosis	5.5
24	(A. G.)	2/ 4/29	52	F	Diabetes	6.0
25	(L. P.)	10/29/28	28	M	No diagnosis	4.8

for thirty-four patients subjected to laparotomy or autopsy in which the pancreas was examined; striking differences in amylase concentration are shown between eleven of them which were "normal" and twenty-three in whom disease of the pancreas was found. Further details of the "normal" patients are summarized in table 3. It will be noted that the condition in a number of them, on account of the presence of jaundice, had been diagnosed as carcinoma at the head of the pancreas. The diagnosis of "normal" pancreas was made by histologic examination in four of these eleven cases at autopsy.

Clinical abstracts of these thirty-four cases in which an operation or an autopsy was performed are appended. In addition, two other patients are described (nos. 35 and 36); on one with pancreatitis, who died, we were unable to perform an autopsy, and in the other pancreatitis was

TABLE 2.—Summary of Observations on Blood Amylase* in Cases Coming to Operation or Autopsy

Case	Normal Pancreas	Diseased Pancreas				Pressure on or Injury to Pancreas	Jaundice
		Chronic Pancreatitis	Acute Pancreatitis	Carcinoma of Pancreas	Pancreatic Cyst		
1	...	25	0
2	5.0	0
3	...	9	0
4	1.0	+
5	150 (A)	0
6	5 (A)	+
7	5.5	0
8	4.5	+
9	...	2.5	0
10	21	0
11	12	0
12	10	+
13	3.1	+
14	6.2	0
15	15	...	0
16	...	7.8	0
17	5 (A)	+
18	...	60	0
19	6.2	0
20	50	...	0
21	4.5	0
22	5.1 (A)	+
23	...	9.5	0
24	25	0
25	...	18.0 (A)	18.0 (A)	18.0	0
26	...	13.6 (A)	+
27	5.0 (A)	+
28	5.2	0
29	...	3.2	0
30	1.5 (A)	+
31	25.0 (A)	+
32	...	4.8 (A)	+
33	7.5 (A)	+
				15.0			
34	12.5 (A)	+

* Numerical values represent units of amylase in blood. "A" indicates that autopsy was performed and that the pancreas was examined histologically. In all other cases diagnosis depended on observations at operation.

TABLE 3.—Cases of Normal Pancreas at Operation or Autopsy

Case	Age of Patient	Clinical Diagnosis	Blood Amylase, Units	Anatomic Observations
2	42	Chronic cholecystitis.....	5.0	Normal pancreas (operation)
6	62	Carcinoma of the pancreas..	4.5	Carcinoma of biliary tract; normal pancreas (autopsy)
7	47	Pancreatic cyst	5.5	Large metastatic carcinoma of liver (from stomach); normal pancreas (operation)
8	45	Carcinoma of the pancreas..	4.5	Acute hepatitis; normal pancreas (operation)
14	48	Duodenal ulcer.....	6.2	Normal pancreas (operation)
17	53	Carcinoma of the pancreas..	5.0	Acute hepatitis; normal pancreas (autopsy)
19	32	Hypertrophy of the bladder; abdominal tumor	6.2	Ovarian cyst; normal pancreas (operation)
21	50	Chronic cholecystitis.....	4.5	Cholecystitis; normal pancreas (operation)
22	48	Stone in the common duct..	5.1	Stone in the common duct; normal pancreas (autopsy)
27	70	Carcinoma of the pancreas..	5.0	Metastatic carcinoma of the biliary ducts and the liver; normal pancreas (autopsy)
28	50	Abdominal tumor.....	5.2	Carcinoma of the gallbladder with metastases to the liver; normal pancreas (operation)

suspected on admission, but hepatitis was indicated by later events. In table 4 is summarized the data for ten cases of chronic pancreatitis. In only two of these cases did we have an opportunity to make histologic examination. The remaining ones are adequately described in the clinical abstracts; that is, seven cases of carcinoma of the pancreas, two of pancreatic cysts, two of acute pancreatitis, and one each of pressure and of injury to the pancreas. At autopsy in the last-named case, a beginning pancreatic cyst was found at the probable site of the injury; this illustrates the pathogenesis of the condition.

REPORT OF CASES

The pancreas in all but two cases (nos. 35 and 36) was examined at operation or at autopsy. The liver function test referred to is that of Graham and Cole.³²

TABLE 4—*Cases of Chronic Pancreatitis*

Case	Age of Patient	Clinical Diagnosis	Blood Amylase, Units	Operative Observations
1	50	Chronic cholecystitis	108/250	Thickened, hard pancreas
3	35	Chronic cholecystitis	93	Enlarged, firm pancreas
9	34	Chronic cholecystitis	25	Enlarged pancreas
10	52	Duodenal ulcer	250	Indurated ulcer perforating into the pancreas
16	33	Chronic cholecystitis	78	Hard indurated pancreas
18	62	Chronic cholecystitis	600	Markedly enlarged and firm pancreas
23	34	Chronic cholecystitis	94	Stony, hard pancreas
26	56	Carcinoma of the pancreas	136	Interacinar infiltration and recent acute inflammation (autopsy)
29	24	Chronic cholecystitis	30	Stony hard pancreas (operation)
32	57	Carcinoma of the pancreas	48	Extensive fibrosis of the pancreas (autopsy)

CASE 1.—In H. F., a laborer, aged 50, admitted to the hospital on Oct 18, 1927, the onset of the condition occurred three years before with epigastric pain after meals, often persisting until the next meal. One week before admission, jaundice appeared, becoming steadily worse.

Examination showed severe jaundice but no evidence of severe pain. The van den Bergh test on admission showed 90 mg. per hundred cubic centimeters. The urine contained bile. The stool was watery and showed some free fat with sudan III stain.

By October 22, the jaundice had cleared considerably. The urine still contained bile.

On October 24, an intravenous cholecystogram showed a faint shadow. The test for liver function showed 40 per cent retention at thirty minutes, the blood amylase value was 108 units.

On November 2, the jaundice was nearly gone. The urine showed no bile. Blood amylase amounted to 25 units.

On November 9, an operation was performed. The gallbladder was greatly thickened and gray. The liver was enlarged; no stones were felt in the common

32 Graham, E. A.; Cole, W. H.; Copher, G. H., and Moore, S. *Diseases of the Gallbladder and Bile Ducts*, Philadelphia, Lea & Febiger, 1928.

duct, but there were many greatly enlarged glands along it. The head of the pancreas was definitely thickened and firm. The gallbladder was removed. The common duct was opened and drained. The patient vomited repeatedly after the operation. Gastric lavage yielded 1,100 cc. of fluid at one time. Death occurred two days after operation; no autopsy was performed.

CASE 2.—E. L. B., a housewife, aged 42, admitted to the hospital on Feb. 14, 1928, had had several courses of antisyphilitic treatment, several years before; the Wassermann reaction was now plus or minus. The onset of the present illness occurred three weeks before admission, with vague dyspepsia. Several days later there was pain in the right upper quadrant of the abdomen with some nausea and vomiting, which continued mildly for a week. The onset of jaundice occurred two weeks before admission; the stools became clay-colored and soft, and the patient had complete anorexia.

Examination showed intense jaundice and tenderness in the right upper quadrant, especially over the gallbladder. The edge of the liver was felt. The test for liver function showed 80 per cent retention. Blood amylase on admission was 0; that is, no diastatic activity could be demonstrated. The van den Bergh reaction on admission was 44 mg. per hundred cubic centimeters. Three weeks later when the jaundice had disappeared, the blood amylase was normal (5.4 units); the van den Bergh reaction was 10 mg. per hundred cubic centimeters, and the result of the liver function test 8 per cent retention. In a cholecystogram there was nonvisualization of the gallbladder.

At operation on March 21, the gallbladder was seen to be slightly thickened, adherent and enlarged. The sentinel gland was three times the normal size, as were the cystic and common ducts. The liver and spleen were adherent to the parietal peritoneum. The pancreas seemed to be normal on palpation. The gallbladder was removed; it contained light brown bile. The patient was discharged on April 16.

CASE 3.—In P. F. K., a housewife, aged 35, admitted to the hospital on Dec. 3, 1928, the onset occurred four or five years before with attacks of severe epigastric pain radiating to the right upper quadrant of the abdomen. A vague pain in the epigastrium was relieved by sodium bicarbonate. The patient lost 60 pounds (27.2 Kg.) in weight in four years. She had had five attacks in the past nine months. There had been no jaundice, but the stools had been clay-colored. Now, for the first time, there was jaundice. Examination showed: jaundice, muscle guard and tenderness in the right upper quadrant under the margin of the ribs. In three weeks, the jaundice was nearly gone, the appetite was better and the pain was absent. The blood amylase value was 9.3 units. The test for liver function showed 22 per cent retention. An operation was performed on Jan. 16, 1929. The gallbladder, on removal, was a thick pinkish gray. Four faceted stones were removed from the common duct which was drained. The pancreas was firm and slightly enlarged. The patient was discharged on February 1.

CASE 4.—In W. C., a policeman, aged 46, admitted to the hospital on Sept. 7, 1927, the condition began two months before with jaundice varying in intensity. One year before admission, while in the hospital for a minor injury, the patient was found to have glycosuria and had been on a diet since. There was slight pain in the right upper quadrant of the abdomen. He had had from ten to sixteen loose stools a day for the past three weeks, and had lost 35 pounds (16.3 Kg.) in weight.

Examination showed a well developed man who was deeply jaundiced. Blood sugar was 146 mg. and serum bilirubin 86.1 mg. per hundred cubic centimeters; the blood amylase value was 1 unit. The test for liver function showed 25 per cent retention.

An operation was performed on September 21. The gallbladder contained 500 cc. of tarry bile. There was a large mass at the head of the pancreas, and small metastases to the liver. A cholecystogastrostomy was performed. The stools contained bile four days after the operation. Recovery was good, and the patient was discharged on October 5.

CASE 5.—In E. M. C., a housewife, aged 67, admitted to the hospital on Dec. 31, 1927, the onset occurred eighteen hours before entrance to the hospital, which was two hours after a large meal; there was severe pain across the upper part of the abdomen and constant vomiting. Morphia had little effect and the patient grew weaker. On entrance, she was pulseless; the temperature was 38.8 C. (101.8 F.), and the white blood cells numbered 4,000. The upper part of the abdomen was rigid and painful. The patient was treated for shock. The blood amylase value was 150 units. The patient grew worse, and died in about six hours. A past history of hypertension and a mild cerebral accident one year before was obtained. The clinical diagnosis rested between coronary thromboses and an abdominal accident although acute pancreatitis was suspected. Autopsy showed acute pancreatitis with fat necrosis confined to the pancreas, acute peritonitis and gallstones.

CASE 6.—R. C., a laborer, aged 62, admitted to the hospital on April 4, 1928, developed pain in the lumbar region three months before. Jaundice appeared two months before admission. With the increase of jaundice, pain diminished and soon disappeared. There was a loss of 25 pounds (11.3 Kg.) in weight. There was no dyspepsia; intense itching was present, but no diarrhea. The blood amylase value was 4.8 units. The test for liver function showed 17 per cent retention.

At operation, several nodules were found along the common duct. The pancreas seemed to be hard. One month later, the patient died. Autopsy showed a normal pancreas and carcinoma of the gallbladder with metastases to the liver and to the glands along the common duct.

CASE 7.—In G. J. W., a farmer, aged 47, admitted to the hospital on March 31, 1928, the onset occurred two months before with dyspnea on exertion; there was no edema. Examination showed: red blood cells, 3,800,000; hemoglobin, 40 per cent; differential count, normal; blood pressure, 120 systolic and 70 diastolic. A tumor was seen and felt in the right upper quadrant of the abdomen; it was probably in the liver; the latter was hard, and its right border was felt distinctly. The guaiac test of the stool repeatedly gave positive results; there was no fat. The heart was normal; an electrocardiogram was negative. A series of gastro-intestinal x-ray pictures revealed an extra-alimentary tumor, independent of the gastro-intestinal tract, which suggested a pancreatic cyst. There was a normal amount of blood amylase (5.5 units). The test for liver function showed 17 per cent retention (normal). On April 14 an operation was performed disclosing a tumor in the liver the size of a grapefruit; it was soft but not fluctuant. There was a mass in the lower third of the greater curvature of the stomach. The lymph glands and a piece of the tumor were removed. The diagnosis was medullary carcinoma of the stomach with metastases to the liver. The patient was discharged on May 1.

CASE 8.—F. L. B., a laborer, aged 45, admitted to the hospital on Oct. 26, 1928, complained of fatigue and anorexia three weeks before. Two weeks before admission, he became yellow. He felt no pain. Examination showed deep jaun-

dice; the edge of the liver was felt below the costal margin. The serum bilirubin was 49 mg. The clinical diagnosis was carcinoma of the pancreas.

The stool was light brown, and acid when tested with litmus. The patient was afebrile during the entire illness. The white blood cells numbered 10,000; the lymphocytes, 37 per cent. Blood amylase amounted to 6.5 units. The tests for liver function showed high retention (80 per cent).

At operation, on November 7, the pancreas proved to be soft and normal in size with a small hard nodule in its head, which did not cause obstruction (retro-peritoneal lymph node?). The liver was swollen. The common duct was not dilated. The gallbladder was moderately distended. A piece of liver which was removed showed acute hepatitis. The patient was discharged on Jan. 28, 1929, well.

CASE 9.—C. J. S., a clerk, aged 34, admitted to the hospital on Oct. 29, 1928, said that she was awakened at 4 a. m., six months before, with pain in the left infracostal region. Chills and night sweats had occurred for six weeks. At the time of admission, she had intermittent infracostal pain on the left side, often lasting for ten days at a time. The patient had a low grade fever, her temperature varying from 99.4 to 100 F. A series of gastro-intestinal x-ray pictures were negative. In the sugar tolerance test, a peculiar rise occurred in two hours. The gallbladder was faintly visualized and showed torsion. Blood amylase amounted to 2.5 units two months before admission; another examination after entrance to the hospital gave the same result.

At operation, on November 15, a chronic inflammation of the gallbladder and appendix was found. The pancreas was definitely enlarged, especially in its body, but it was not very hard (lipomatosis of the pancreas?). The patient was discharged on November 30.

CASE 10.—G. H. B., a mechanic, aged 52, gave a meager history of gradually increasing vomiting for the previous six months. Two weeks before admission, roentgen examination showed marked six-hour retention and a long narrow duodenal cap. On admission, the patient was drowsy and weak. The nonprotein nitrogen amounted to 166 mg. per hundred cubic centimeters, and the secretion of phenolsulphonphthalein was 5 per cent in two hours. Blood amylase amounted to 21 units. Fluids administered parenterally, and high caloric liquid feedings were given; in fourteen days, the nonprotein nitrogen and the phenolsulphonphthalein were normal, and the general condition was markedly improved. Blood amylase showed 21 units. At operation, a large duodenal ulcer adherent to and perforating into the pancreas was found.

CASE 11.—J. A. H., aged 61, admitted to the hospital on March 21, 1928, had a huge hydronephrosis of the right kidney. No gallbladder shadow was visible. Blood amylase amounted to 12.5 units. A right nephrectomy was performed on April 2. A large dilated sac was observed to press on the gallbladder and the pancreas. The patient was discharged on April 19.

CASE 12.—J. W. S., aged 58, admitted to the hospital on Feb. 29, 1928, developed nausea and general abdominal discomfort eight weeks before admission; he became worse, and in one week his color was yellow. He had had diarrhea for several weeks. One attack of transient pain had been felt in the upper right quadrant of the abdomen. The Wassermann reaction was negative. On three examinations with sudan III stain, the stool showed fat; no bile was found. Sugar was repeatedly shown in the urine from March 1 to 15; it then disappeared. Blood sugar amounted to 116 mg. per hundred cubic centimeters, blood amylase to 10.7 units. The test for liver function showed 23 per cent retention.

At operation, a hard mass was found in the head of the pancreas, and a cholecystogastrostomy was performed. There was no bile in the stool on discharge, March 27, although the jaundice had cleared up considerably.

CASE 13.—P. J. S., a foreman, aged 37, first admitted to the hospital on Nov. 4, 1926, gave a history of intermittent and irregular attacks of jaundice for one year, with a loss of 35 pounds (16.3 Kg.) in weight and from five to six stools a day. Examination showed an enlarged liver and jaundice. The test for liver function yielded 17 per cent retention. The clinical diagnosis was cirrhosis of the liver. An operation was advised but was refused by the patient. The patient was discharged on November 12, but was readmitted on July 6, 1927. Intermittent attacks of jaundice had continued, with greater severity. The test for liver function showed 17 per cent retention. Blood amylase amounted to 3.1 units. An operation on July 10 revealed a large tumor in the head of the pancreas. The patient died on July 15.

CASE 14.—In R. M., the blood amylase amounted to 62 units. An operation was performed for duodenal ulcer. A gastro-enterostomy was also performed. The pancreas was of normal appearance and consistency. Recovery was uneventful.

CASE 15.—R. G., a colored laborer, aged 46, was admitted on April 13, 1927, with a history of pain around the umbilicus after meals for the previous one and a half years. The patient had lost 35 pounds (16.3 Kg.) in weight. Examination showed a tumor in the upper part of the abdomen, that was cystic, rounded and movable. A series of gastro-intestinal x-ray pictures showed an extra-alimentary tumor. Blood amylase amounted to 14.7 units. An operation was performed on April 25. A large pancreatic cyst was marsupialized. The fluid contained 300 units of amylase per cubic centimeter. The blood amylase value, three days after the operation, was 6.7 units. The wound healed rapidly, and the patient was discharged on May 7. He was readmitted on October 7 with a history of excellent health until the onset of pain, nausea and vomiting two weeks before. Examination showed evidence of chronic cholecystitis. An operation was performed on November 11. The gallbladder and stones were removed. The pancreas was difficult to palpate but the head seemed to be somewhat indurated.

CASE 16.—G. S., a housewife, aged 33, admitted to the hospital on March 28, 1928, gave a history of severe, nearly painless jaundice, occurring seven years before and lasting for eight months. She had had intermittent attacks of jaundice of short duration for the past few years, and attacks of pain requiring morphine. Examination showed tenderness to the right of the umbilicus and over both twelfth ribs. The blood amylase amounted to 7.8 units. The test for liver function showed 9 per cent retention (normal). At operation, on April 16, no gallbladder and no stones were found. The common duct was drained; the pancreas was hard and indurated. The patient was discharged on April 21.

CASE 17.—H. F., a housewife, aged 53 (referred by Dr. A. Goldman), gave a history of diabetes of three years' duration, controlled by diet without insulin. The onset of the present illness occurred one month before admission to the hospital, with chills and fever which subsided in ten days. Ten days later jaundice was noted, becoming increasingly severe. Fever returned and rose as high as 104 F. There was vomiting, and pain in the joints, but no abdominal pain. Examination showed deep jaundice, a large mass in the right upper quadrant of the abdomen, probably in the liver, which was hard but not tender. The urine contained bile but no urobilin. The test for liver function showed 75 per cent retention. The clinical diagnosis was stone in the common duct, or carcinoma of the pancreas. The blood amylase amounted to 5 units. An operation revealed

a normal pancreas, an enlarged liver, and a normal gallbladder and ducts. At the neck of the gallbladder, numerous enlarged glands were found which were removed. The patient died five days later. At autopsy, acute degenerative hepatitis and nephritis were found. The pancreas was normal.

CASE 18.—H. W. B., a housewife, aged 62 (referred by Dr. W. F. Peterson), gave a history of low grade colitis for eighteen years; and attacks of pain in the epigastrium, vomiting and clay-colored stools at intervals for the past year. Examination showed only a little albumin and hypertensive myocarditis; a cholecystogram showed no shadow. The blood amylase amounted to 60 units. An operation, performed on Oct. 15, 1928, showed evidence of an ulcer near the pylorus. A posterior gastro-enterostomy was performed; the appendix was removed and the gallbladder was emptied of many stones and drained. The pancreas was markedly enlarged and firm. The course was uneventful until eight days after operation when the patient suddenly died. No autopsy was performed.

CASE 19.—T. J. J., a housewife, aged 32, was admitted to the hospital on Feb. 16, 1929, for the cure of an exstrophy of the bladder which she had had since birth. A large abdominal tumor was found during the routine examination; it was freely movable but firm and indefinitely outlined. Roentgen examination showed an extra-alimentary tumor. A pancreatic cyst was suspected. The blood amylase amounted to 6.2 units. At operation, on March 4, the tumor was found to be a huge, bilateral ovarian cyst. The pancreas was normal. The patient was discharged on March 20.

CASE 20.—M. E. F., a housewife, aged 44, admitted to the hospital on Oct. 28, 1927, gave a history of irregular attacks of pain in the epigastrium for the past ten years, with nausea, belching and vomiting. An abdominal swelling observed four weeks before admission increased in size. Examination showed a huge, tense, cystic tumor in the epigastrium. The blood amylase amounted to 29 units on October 28, and 50 units on November 2. A series of gastro-intestinal x-ray pictures revealed an extra-alimentary tumor, probably a pancreatic cyst. At operation, on November 4, the large cyst was drained of 2,000 cc. of fluid; a large piece of necrotic tissue was removed and the cyst was marsupialized. The cystic fluid contained 1,200 units of amylase. No bile or trypsin was demonstrable. The wound healed slowly but satisfactorily. Recovery was uneventful, except for persistent tachycardia and weakness (pancreatic asthenia?). On November 9, blood amylase amounted to 10 units. The patient was discharged on December 3.

CASE 21.—M. S. Y., a housewife, aged 50, was admitted to the hospital on Jan. 9, 1928. The onset occurred fifteen months before admission, with dyspepsia and cramping pain in the epigastrium. Since then, the patient had lost 50 pounds (22.6 Kg.). Results of an examination were negative. A cholecystogram revealed no shadow. A series of gastro-intestinal x-ray pictures were negative. Blood amylase amounted to 4.5 units. In an operation, on Jan. 12, 1928, a diseased gallbladder and a number of stones were removed. The pancreas felt normal. The patient was discharged on January 27.

CASE 22.—C. L. H., a laundress, aged 48, admitted to the hospital on July 14, 1927, gave a history characteristic of disease of the gallbladder. Examination showed jaundice and an enlarged, tender liver. The test for liver function showed high retention of dye (80 per cent). Blood amylase amounted to 5.1 units. An operation, on July 19, revealed a stone in the cystic duct and several stones in the common duct, which were removed. White bile was found above the obstruction. A cholecystectomy was performed; the pancreas was normal. Death occurred in twelve hours. Autopsy revealed 1,400 cc. of blood in the peritoneal

cavity, chronic hepatitis and pulmonary edema. The pancreas was normal grossly, and in section showed only a slight increase in interacinar connective tissue.

CASE 23.—In A. A. L., a housewife, aged 34, admitted on Jan. 24, 1929, the history and examination disclosed symptoms characteristic of chronic disease of the gallbladder. Blood amylase amounted to 9.4 units. At operation, on February 1, the gallbladder and several stones were removed. The pancreas was as stony hard as if it were affected with carcinoma. The patient was discharged on February 15.

CASE 24.—W. H., a laborer, aged 42, admitted to the City Hospital on Nov. 28, 1927, had experienced sudden pain to the right of the umbilicus two days before; it became worse, and the patient vomited persistently. The abdomen was scaphoid; there was rigidity in its upper portion. The white blood cells numbered 17,400. Generalized pain was present. At operation, free blood was found in the peritoneal cavity; there were many flecks of fat necrosis in the omentum. The pancreas was enlarged and hemorrhagic. The lesser peritoneal cavity was drained, and the patient developed signs of tetanus and died on December 5. Blood amylase, two days after operation, amounted to 25 units.

CASE 25.—G. K., a clerk, aged 21, was admitted to the City Hospital on Dec. 4, 1928, as an emergency case with a history of severe pain in the epigastrium and of persistent vomiting for forty-eight hours. Six months before, he was in an automobile accident and sustained a crushing blow in the upper part of the abdomen following which he vomited persistently. Operation revealed a large mass, probably a hematoma, in the region of the pancreas. Blood amylase a few weeks later amounted to 16.6 units. The patient was discharged as improved, but had attacks of pain and vomited at irregular intervals, once vomiting blood. Blood amylase, on November 1, amounted to 16.8 units.

On this admission he presented the picture of an acute abdominal condition. His abdomen was distended and rigid, especially in the upper half, and was exquisitely tender to pressure. The temperature was 102 F., the pulse rate 130. The white blood cells numbered 14,000, later 42,000. In view of the previous history, acute pancreatitis was suspected. Blood amylase, however, was but 7.1 units. At operation the mass noted at the first operation was found; the omentum around it showed one large whitish area of old, organizing fat necrosis. No other fresh areas of fat necrosis were seen. The peritoneal cavity contained about 2 liters of clear straw-colored fluid. The loops of small intestine were distended, but no peritonitis was present. The mass was incised and found to be solid fibrous inflammatory tissue in which several loops of collapsed small bowel were seen. Further exploration revealed no evidence of abscess or softening. The general condition of the patient precluded further work, and an enterostomy was performed with a rubber tube; the wound was closed with through-and-through ligatures. After a stormy convalescence, the patient recovered and gained 30 pounds (13.6 Kg.) in weight. Four months later, he became suddenly ill and died in a week with generalized petechiae. Autopsy revealed a vegetative endocarditis. The pancreas was small and hard, and there was a cyst at the head, about 5 cm. in diameter, containing clear fluid. Section of the gland showed advanced cirrhotic changes. Blood amylase, one week before death, amounted to 18.5 units.

CASE 26.—In M. F., a housewife, aged 56, admitted to the City Hospital on Dec. 28, 1928, the onset occurred two weeks before admission, with nausea, anorexia, dyspepsia and increasing jaundice. There was a loss of 25 pounds (11.3 Kg.) in weight. Examination showed a sick woman, with jaundice, who was fairly well nourished and had many petechiae. A series of gastro-intestinal x-ray pictures

showed nothing abnormal. Blood amylase amounted to 13.7 units. A test of liver function showed 15 per cent retention. The Wassermann reaction was negative. The phenolsulphonphthalein test gave normal results. Death occurred suddenly on Jan. 19, 1929. The clinical diagnosis was carcinoma of the pancreas. A limited autopsy revealed no carcinoma. The pancreas showed old interacinar fibrosis with, a recent acute inflammatory process.

CASE 27.—In F. F., a laborer, aged 59, admitted to the City Hospital on Jan. 18, 1929, the onset occurred two months before admission, with pain in the chest and the upper part of the abdomen, and with increasing jaundice. Examination showed a deeply jaundiced patient with an irregular mass in the right upper quadrant of the abdomen, probably in the liver. A series of gastro-intestinal x-ray pictures were negative. Blood amylase amounted to 5 units. Operation showed multiple nodules in the liver, and a mass in the region of the head of the pancreas. The patient died several days later. Autopsy showed that the mass felt at operation was a large retroperitoneal node, and was not connected with the pancreas. Sections of the pancreas showed normally formed acini with no sign of obstruction of the ducts. There were numerous nodules along the common duct and in the liver to account for the jaundice. Sections showed the tumor to be of the neuroganglionic type, probably arising from retroperitoneal nerve tissue.

CASE 28.—F. M. M., a housewife, aged 59, admitted to the hospital on Jan. 15, 1929, gave a history of weakness for the past year, enlargement of the epigastrium and discoloration of the skin. Examination revealed a prominent abdomen, a hard, nodular, enlarged liver and an enlarged spleen. All laboratory tests gave negative results. Biopsy of the skin showed no iron pigment. The liver function test showed normal retention (18 per cent). Blood amylase amounted to 5.2 units. A series of gastro-intestinal x-ray pictures were negative. A cholecystogram did not give visualization. At operation, under local anesthesia, on January 28, the liver was found to be tremendously enlarged and to contain multiple metastases. The gallbladder was edematous and contained stones. The stomach could not be examined well on account of pain. The pancreas felt normal. Biopsy showed adenocarcinoma, probably from the gallbladder. The patient was discharged on February 21.

CASE 29.—C. M., a housewife, aged 24, admitted to the City Hospital on Feb. 14, 1928, gave a history of intermittent attacks of severe pain in the right upper quadrant of the abdomen, with vomiting. Examination showed an obese woman, slightly jaundiced, with tenderness over the entire abdomen, especially in the right upper quadrant. Blood amylase amounted to 3.1 units. A cholecystogram showed a faint shadow. At operation, on February 27, a diseased gallbladder and several stones were removed. There was no stone in the common duct. The probe was passed into the duodenum from the opening in the duct. The pancreas was hard throughout its entire extent, and felt like carcinoma.

CASE 30.—In J. S. (referred by Dr. John Hotz), a laborer, aged 56, admitted to the City Hospital on Feb. 1, 1929, the onset occurred six months before admission, with gradually increasing, painless jaundice. The patient had diarrhea "severe enough to take medicine for it." Five weeks before admission, swelling of the ankles was noted. Three weeks later there was swelling of the abdomen and dyspnea. Examination showed a distended abdomen. Paracentesis on numerous occasions yielded from 5,000 to 6,000 cc. each time. A series of gastro-intestinal x-ray pictures were negative. Blood amylase amounted to 1.1 units. The Wassermann reaction was negative. Jaundice grew progressively more intense. Death occurred two months after admission. A limited autopsy revealed a hard mass at

the head of the pancreas. Microscopic examination showed vacuolization and atrophy of the acini.

CASE 31.—M. B. M., a man 48 years of age, admitted on March 22, 1929, gave a history of treatment for syphilis; the Wassermann reaction was now negative. The onset occurred six weeks before admission, with severe diarrhea. Two weeks later the gradually increasing jaundice began; there was no pain. Examination revealed extreme icterus, some rigidity and tenderness in the epigastrium; edema of the lower part of the legs, and ascites. The test for liver function showed 18 per cent retention (normal). In two examinations, blood amylase amounted to 25 and 30 units, respectively. At operation, on April 12, 3 liters of ascitic fluid was removed; an enlarged gallbladder and hobnail liver were observed. An omentopexy was performed. Death occurred three days later. Autopsy revealed hepatic cirrhosis, and carcinoma at the orifice of the common and pancreatic ducts, obstructing both. The pancreas on section showed pink-staining acini, tremendously dilated ducts and early hemorrhagic pancreatitis.

CASE 32.—In W. H. W., a laborer, aged 57, admitted to the hospital on March 19, 1928, the onset of the condition occurred seven weeks before admission, with a progressive increase in jaundice and dull pains in the lower portion of the chest and back, gradually becoming more severe. Constipation was marked. Examination showed marked jaundice and a large tumor in the right upper quadrant of the abdomen, probably the liver, which was nodular and extended down into the umbilicus. The Wassermann reaction was four plus. The test for liver function showed 17 per cent retention. Blood amylase amounted to 4.8 units. A series of gastro-intestinal x-ray pictures showed an extra-alimentary tumor, and hydrops of the gallbladder (?). The patient was discharged on March 28. Death occurred on May 9. An autopsy, performed by Dr. D. L. Harris, showed an enormously dilated gallbladder, and a nodular, hard, fibrotic pancreas which constricted the lower end of the common duct with a fibrous band. Section of the gland showed no carcinoma; there was only an extensive fibrosis with scattered groups of acinar cells.

CASE 33.—In W. J., a colored laborer, aged 57, admitted to the hospital on March 12, 1929, the onset of the condition occurred six weeks before admission, with pain in the epigastrium, increasing jaundice, and constipation. There was a loss of 100 pounds (45.3 Kg.) in weight during this time from a usual weight of 220 pounds (99.8 Kg.). Examination showed intense jaundice, glycosuria, and 220 mg. of blood sugar per hundred cubic centimeters, a condition that was soon controlled with diet and insulin. The abdomen was soft; there was a tumor in the epigastrium, probably in the gallbladder. Blood amylase, on March 15, amounted to 7.5 units; on April 5, 5 units. At operation, on April 12, a tumor was felt in the head of the pancreas; an enlarged gallbladder was anastomosed to the stomach. Death occurred three days later. The autopsy showed a carcinoma in the head of the pancreas through which the pancreatic duct could be followed from the tail to the duodenum without apparent obstruction. The tumor, however, occluded the lower common duct. Section of the body of the pancreas showed extensive fibrosis of the gland with many normal-staining acinar cells.

CASE 34.—In C. D., a colored laborer, aged 49, admitted to the hospital on March 27, 1929, the onset occurred two months before admission, with dull pain in the epigastrium, bloating constipation, increasing jaundice and the loss of 60 pounds (27.2 Kg.) in weight. On examination the liver edge was felt. Other observations were: a distended gallbladder (?), deep icterus, glycosuria, a Wassermann reaction of four plus, blood sugar 216 mg. per hundred cubic centimeters, and

an icteric index of 150. The stool showed fatty acid. A series of gastro-intestinal x-ray pictures revealed a retroperitoneal tumor. Blood amylase, on April 1, amounted to 12.5 units; on April 16, 10.8 units. On May 8 the patient died suddenly. Autopsy showed a large tumor in the head of the pancreas compressing the common bile duct and the main pancreatic duct; the latter was dilated to the size of a finger. Section of the tail of the pancreas showed many normal-staining acini, and general dilatation of the small ducts.

CASE 35.—M. M., a housewife, aged 48, admitted to the hospital on Oct. 23, 1928, developed jaundice one month before admission, which gradually increased. She lost 33 pounds (14.9 Kg.) in weight. There had been pain along the costal margin for six months, vomiting for one week. Examination showed a blood sugar of 0.294 Gm. per hundred cubic centimeters. The gastric contents after a test meal were 63 degrees total acid. The serum bilirubin on admission was 21; two days later, 40; three days later, 83, and three days later, 65. Blood amylase, on October 31, amounted to 1.9 units and on November 2 to 1.8 units. The patient died suddenly on November 19. No autopsy was performed.

CASE 36.—A. G. A., a housewife, aged 36, was admitted on Oct. 30, 1928, as an acute emergency case with a history of vomiting daily for the previous two weeks. There had been pain in the epigastrium, loss of weight, and a temperature of from 101 to 103 F. Examination showed an acutely ill woman with jaundice and much spasm in the epigastrium and right upper quadrant of the abdomen. An indefinite mass in the epigastrium was not outlined because of muscle spasm. The condition was thought to be of pancreatic origin, but the blood amylase was normal (4.3 units). A series of gastro-intestinal x-ray pictures were negative. The jaundice and fever cleared, and a history of alcoholism was then obtained. The diagnosis was hepatitis in alcoholic psychosis. The patient was discharged on December 18.

COMMENT

The immediate inference to be drawn from the data herein presented is that there is a definite correlation between the concentration of blood amylase and the presence or absence of disease in the pancreas, thus bearing out the experimental evidence that this ferment in the blood is largely of pancreatic origin. The main application of our data, however, concerns the addition of a valuable aid in the diagnosis of diseases of the pancreas which are frequently difficult of clinical detection.

A brief summary of our observations is as follows: In thirty-six patients, the blood amylase was found to lie between 4.3 and 6.8 units. In eleven of these, the pancreas was either felt at operation or examined microscopically after autopsy and found to be normal (table 3). The remaining twenty-five were patients convalescent from a variety of conditions (table 1). In twenty-two patients, abnormal concentration of blood amylase was found; in fifteen of them increased values ranging from 7.8 to 150 units but in seven cases values below normal, that is, from 0.5 to 3 units. In twenty-one of these twenty-two cases which showed abnormal values, disease of the pancreas was found, either at operation or at autopsy, distributed among the conditions as follows: chronic pancreatitis ten cases (table 4), carcinoma of the pancreas

seven, acute pancreatitis two, pancreatic cyst two, injury to the pancreas one, and pressure on the pancreas one. All cases in which an operation or an autopsy was performed are summarized in table 2.

Certain limitations of these observations must be noted. Our basis for diagnosis of disease in the pancreas in the majority of the cases was dependent on the data obtained at operation. The reliability of palpation or even of inspection of this small inaccessible organ during laparotomy may be questioned seriously. The liver, large and visible as it is, was for a long time overlooked as the site of inflammatory changes. It was only after the extensive observations³² in this clinic, that the frequency of hepatitis was established and its importance first realized. But much of the evidence rested on the microscopic examination of tiny pieces of liver removed at operation. It is, of course, more difficult to perform biopsy on the pancreas. J. H. Nicoll,³³ however, a British surgeon, described a number of cases in which he has excised a wedge of tissue from the pancreas through an opening in the gastrocolic omentum and was enabled, thereby, to make a diagnosis of pancreatitis from the microscopic examination of the tissue removed in seven cases in which the clinical diagnosis was entirely different. He pointed out also the possible unreliability of a palpatory diagnosis of pancreatic disease at operation. In one case of our series (no. 27), autopsy showed that a mass in the region of the head of the pancreas, felt at operation and diagnosed as a carcinoma at the head of the pancreas, was in reality an enlarged retroperitoneal lymph gland, and that the pancreas was normal microscopically. In twelve cases of our series we obtained microscopic examinations of the pancreas (nos. 5, 6, 17, 22, 25, 26, 27, 30, 31, 32, 33 and 34 which came to autopsy). It is significant that in ten of them there was a complete confirmation of the observations on blood amylase. The other two (cases 32 and 33) will be discussed later.

A possible limitation in the method described lies in the making up of the starch suspension, since different preparations give solutions of different viscosities and varying rates of hydrolysis. By using the same batch of starch and by making a fresh preparation of it each time in the same way, uniform results were obtained. In our experience, the method was accurate to within 10 per cent in repeated determinations on the same specimen. We are now working on methods for preparing a more standard and more simple solution of starch.

The existence of jaundice, *per se*, has no effect on the amylolytic activity of blood. This was determined by actually adding bile to normal serum and finding no alteration in its diastatic power. Moreover, in five cases of hepatogenous icterus in which the pancreas was *not*

33. Nicoll, J. H.: *Brit. M. J.* 2:625, 1919.

affected, "normal" amylase values were obtained (table 3, nos. 6, 8, 17, 22 and 27). This fact has enabled us to exclude the pancreas in a number of cases of painless jaundice when the clinical diagnosis pointed to carcinoma of the pancreas.

In a number of cases, too, the amylase determination gave the only indication of pancreatic disease, the clinical evidence being either inconclusive or indicative of another diagnosis (nos. 5, 13 and 15). In one case a normal amylase value ruled out a possible pancreatitis and subsequent events showed the inference to be correct (case 36). In another instance (no. 7) an abdominal tumor, supposed from roentgen examination to be a pancreatic cyst (blood amylase normal), was found at operation to be a large metastatic nodule from a carcinoma of the stomach.

The significance of the low amylase values obtained in this series of cases can easily be surmised. From the experimental evidence already mentioned one might interpret it as an indication of more or less complete atrophy of the acinar cells, for if the amylase of the blood is derived from these cells, atrophy would probably bring about this decrease. In only one case with a low value (no. 30) did we have an opportunity of examining the pancreas microscopically. In this case of carcinoma of the pancreas the blood amylase value, two weeks before death, was only 1.5 units or from about one-third to one-fourth the normal value. On section, this pancreas showed extensive involvement of the acini many of which were replaced by fat cells, the others being necrotic or completely fibrosed. The islets of Langerhans appeared normal. Of the other six cases of decreased amylase concentration, four (nos. 4, 9, 13 and 29) showed changes at laparotomy. The fifth patient (no. 35) had both glycosuria and jaundice, but died; no autopsy was obtained. The last case (no. 2) is more difficult to explain. On admission the patient had almost no amylolytic activity in the blood and showed intense jaundice. Operation was performed five weeks later, after the jaundice had disappeared. At this time the blood amylase was normal. The laparotomy revealed chronic hepatitis and what was taken to be a normal pancreas. It perhaps illustrates the rapid power of the pancreas to recover from a severe degree of inflammation.

The significance of the increased amylase in the blood seems clear. Obstruction to the ducts leading to increased absorption of pent-up ferments into the blood finds experimental corroboration in the evidence already cited. This is probably the mechanism in the cases of obstruction due to carcinoma (as well shown in no. 31) unless the process has led to atrophy of the acini. Atrophy probably occurred in three of our seven cases and accounts for the low amylase value in them. In a pancreatic cyst there is either pressure on the gland leading to a generalized occlusion of the ducts or an increased absorption of ferments from the

lining of the cyst; for the fluid in the cyst in our two cases contained 300 and 1,200 units of amylase or from sixty to 250 times the concentration in normal blood. The inflammatory process in chronic pancreatitis probably leads to obstruction of the smaller ducts by scar tissue. Interlobular and interacinar fibrosis of this kind has been described by Opie³⁴ and others. Experimentally we have observed this same histologic change in the pancreas of dogs intubated for the collection of pancreatic juice³⁵ whenever the secretion became infected. Although no obstruction could be found at autopsy, the flow of pancreatic juice diminished markedly and an increase in the blood amylase was demonstrable in each case. If, however, the fibrosis progresses to completion so that all the acini are replaced with fibrous tissue, one would expect a diminution in the blood amylase. This is probably the explanation of the low value in case 29. In certain cases, pancreatic acini may become replaced by fat, the so-called lipomatosis of the pancreas as described by Balo and Ballon.³⁶ In this event a similar lowering of the ferment in the blood might occur, thus explaining the enlarged soft pancreas in case 9. Only by histologic examination, however, could such a correlation be really established. In acute pancreatitis there is an abnormal absorption of ferments into the blood because of acute inflammatory changes and tryptic digestion of the walls of the ducts, so that the secretion instead of flowing on into the duodenum makes its way into the surrounding tissues and into the blood and lymphatics.

Disease of the pancreas may thus affect the concentration of blood amylase in two opposite directions: By obstruction of the outflow of pancreatic juice, there is an increased resorption of ferments into the blood; by atrophy of the acini there is a lowering of the normal resorption due to a lowered ferment production. In the former case the blood amylase is high, in the latter low. In a case of progressive obstruction leading to atrophy it is easy to see that a point would be reached when the blood amylase would be neither high nor low; that is, it would be "normal." A mechanism of this kind probably explains the normal observations on blood amylase in cases 32 and 33 in which marked disease of the pancreas was found at autopsy. In case 33 the first determination was slightly elevated (7.5 units); a second one three weeks later was normal (5). It is probable that had the patient lived, the amylase value would have become subnormal, since on section the gland appeared to be well on the way to atrophy. In case 32 our only determination was made two months before death.

34. Opie, E. L.: *Diseases of the Pancreas*, Philadelphia, J. B. Lippincott Company, 1911.

35. Elman, R., and McCaughan, J. M.: *J. Exper. Med.* **45**:561, 1927.

36. Balo, J., and Ballon, H. C.: *Surg. Gynec. Obst.* **48**:1, 1929.

The influence of renal insufficiency on blood amylase deserves special mention. Some observers have claimed that amylase is retained, along with other substances, in cases of nitrogen retention (Stafford and Addis,²⁵ Meyer and Killian,²⁹ and Lawis and Mason).³⁰ Some experimental evidence indicates, on the contrary, that renal activity does not influence blood amylase. Thus van de Erve³⁷ found no change in the concentration of blood amylase following (a) ligation of the renal arteries, (b) induced polyuria and (c) anuria. In only one of our cases (no. 10) did we have an opportunity of making any observations on this problem. The high blood amylase (21 units) remained the same after a high nonprotein nitrogen content (120 mg. per hundred cubic centimeters) found in the blood on admission had been brought to normal limits by forced fluids. At operation a duodenal ulcer perforating into the pancreas was found.

SUMMARY

The concentration of amylase in adult human plasma was determined in sixty patients by means of a new method. Uniform values (from 4.3 to 6.8 units) were found in a series of twenty-five unselected cases in which there was no suspicion of disease of the acini of the pancreas. The same "normal" range of values was found in eleven additional cases in which the pancreas was actually examined and found to be normal, seven of these by palpation at operation and four by microscopic section after autopsy.

Definite deviations from this "normal" range were found in twenty-one of twenty-three cases in which disease of the pancreas was found either at operation or at autopsy. In most instances a moderate or marked increase in the blood amylase was found (from 7.8 to 150 units); in some a definite decrease occurred (from 0.5 to 3.1 units). The significance of these observations has been pointed out.

The determination of blood amylase has been of undoubted clinical value in a number of cases both in excluding suspected disease of the pancreas and in adding conclusive confirmatory evidence when the clinical picture was indefinite or vague. Jaundice, per se, has no influence on the amylolytic power of human blood unless disease of the pancreas is also present.

37. Van de Erve, J.: *Am. J. Physiol.* **29**:182, 1911.

FRACTURES OF THE TRANSVERSE PROCESSES OF THE LUMBAR VERTEBRAE

A REPORT OF THIRTY-THREE CASES *

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LOS ANGELES

My purpose in this paper is to reemphasize certain points in the mechanism, etiology, symptoms and diagnosis of fractures of the transverse processes of the lumbar vertebrae, and to report observations, especially with reference to union and the duration of disability, on a series of thirty-three cases seen in industrial practice over a period of two years.

Little or no mention was made of these fractures in textbooks on orthopedics and fractures by Taylor,¹ Albee,² Scudder,³ Roberts and Kelly,⁴ Preston,⁵ Stimson,⁶ Jones and Lovett,⁷ Cotton⁸ and Whitman.⁹ Speed¹⁰ and Hoffman¹¹ reported cases that were due to muscular action. Rhys,¹² Hartwell,¹³ Davis¹⁴ and Bierman¹⁵ have written on the diag-

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* From the Golden State Hospital.

1. Taylor, H. L.: Orthopedic Surgery, New York, D. Appleton & Company, 1909.

2. Albee, F. H.: Orthopedics and Reconstruction Surgery, Philadelphia, W. B. Saunders Company, 1919.

3. Scudder, C. L.: The Treatment of Fractures, Philadelphia, W. B. Saunders Company, 1923 and 1926.

4. Roberts and Kelly: Fractures, Philadelphia, J. B. Lippincott Company, 1916.

5. Preston, Miller: Fractures and Dislocations, St. Louis, C. V. Mosby Company, 1915.

6. Stimson, Louis: On Fractures and Dislocations, Philadelphia, Lea & Febiger, 1910, p. 150.

7. Jones, Sir Robert; and Lovett, R. W.: Orthopedic Surgery, New York, William Wood & Company, 1923, p. 316.

8. Cotton, F. J.: Dislocations and Joint Fractures, Philadelphia, W. B. Saunders & Company, 1924, p. 142.

9. Whitman, Royal: Treatise on Orthopedic Surgery, Philadelphia, Lea & Febiger, 1927, p. 118.

10. Speed, Kellogg: Fractures and Dislocations, Philadelphia, Lea & Febiger, 1916, p. 251.

11. Hoffman: Med. Klin., 1914, vol. 10, quoted by Speed (footnote 10).

12. Rhys, O. L.: Pseudofracture of Transverse Processes of Lumbar Vertebrae, Brit. M. J., May 24, 1913; Healed Fractures of Transverse Processes of Vertebra, Ibid. 1:873 (May 14) 1927.

nosis and etiology of these fractures, considering both direct trauma and indirect muscular action and also the simulation of fracture by accessory lumbar ribs. Kennedy¹⁶ reported ten cases and reviewed the reported cases from the earliest (that of Ehrlich) in 1908 up to 1927.

ETIOLOGY

Knowledge of the embryology, anatomy and physiology of the structures of the back aids in determining the mechanism in fracture of the transverse processes of the lumbar vertebrae. The transverse and articular processes arise from the neural processes immediately behind the costal processes. In the lumbar region the latter become parts of the vertebrae. One center of ossification for each vertebral arch appears about the seventh week (Cunningham¹⁷). Of the secondary epiphyseal centers which appear at puberty there is one at the lateral extremity of each transverse process. Fusion of these with the shaft of the bone does not occur until the twenty-fifth year.

Anatomically, the transverse processes are slender, and quite thin vertically, and point horizontally and slightly backward and upward. The cancellous bone of their broad bases withstands greater stress than the more compact shafts; hence most fractures occur through the latter. The fifth and first processes are less frequently injured because of their protected positions. The quadratus lumborum muscles, arising from the fixed iliac crest and inserted into the tips of the transverse processes and the medial half of the twelfth rib, flex the lumbar spinal column laterally and draw the twelfth ribs downward. The longissimus dorsi, multifidi, intertransversarii and psoas majori act principally on the pedicles, mammillary processes and bodies of the vertebrae.

How are fractures of the transverse processes produced? That they result from direct violence or blows directly over the processes is self-evident. Upward dislocation of the ilium may fracture the fifth process; one case of this kind is reported in this series. That indirect violence from muscular action may fracture these processes was not recognized by Stimson⁹ and was questioned by Rhys,¹² who regarded these separated transverse processes as developmental anomalies. Though he reported many cases with fractures unilaterally and bilaterally, he did not think that "strain distinct from direct violence can fracture these

13. Hartwell, J. B.: *Colorado Med.* **16**:78 (April) 1919.

14. Davis, G. G.: *Fractures of Transverse Processes of Lumbar Spine*, *Surg. Gynec. Obst.* **33**:272 (Sept.) 1921.

15. Bierman, N. J.: *Am. J. Roentgenol.* **10**:456 (June) 1923.

16. Kennedy, R. H.: *Fracture of Transverse Processes of Lumbar Vertebrae*, *Ann. Surg.* **85**:519 (April) 1927.

17. Cunningham: *Text Book of Anatomy*, New York, William Wood & Company, 1919, p. 104.

processes" and yet he did not see how (nor do I) "an injury (a force applied directly) could fracture transverse processes on both sides without also fracturing the spinous processes." He believed that considerable direct force was necessary to break a bone protected as these processes are and doubted fracture if there were no local external signs of injury.

Speed,¹⁰ on the other hand, regarded many of these fractures as "caused by forcible contraction of the psoas and quadratus lumborum and longissimus dorsi muscles." He pointed out that fractures occur bilaterally and when the person is lifting heavy weights or is subjected to sudden strain in the forward flexed position. Nineteen cases due to muscular action were cited by him (Lange, Ehrlich, Hoglund, Hoffman¹¹). Jones and Lovett⁷ and Cotton⁸ recognized both direct violence and indirect muscle strain as causes. Davis¹⁴ believed that in practically all of these fractures the mechanism is one of indirect violence by muscular action. One of Davis' cases resulted from buckling or jack-knifing in a coal slide; there was a downward dislocation of the twelfth rib on the side of the fractures, again suggesting muscular action as the cause. In another case, fracture of three transverse processes followed an attempt to lift a loaded tram off a fellow workman. Kennedy¹⁰ reported ten cases due to direct violence and cited Hoglund's three cases due to indirect muscular action. Two of the latter occurred while the patients were riding bicycles; the third while lifting a weight in a stooping attitude. In my opinion it must be recognized that violent contraction of the quadratus lumborum and other muscles of the back, with the thorax and pelvis both fixed, can and does result in fracture of one or more transverse processes. Separation of an ossific (epiphyseal) center, as suggested by Rhys, would not seem plausible after the twenty-fifth year of age.

In the thirty-three cases reported in this paper, direct external violence was responsible for the injury in eighteen instances, direct internal violence (ilium) in one and indirect muscular action in two. In two cases both direct and indirect violence were considered to have acted. In seven cases the mechanism could not be determined, as accurate histories of injury were not obtained. In two cases the diagnosis of fracture was questionable.

SYMPTOMS AND DIAGNOSIS

The most important diagnostic sign is tenderness localized immediately over the injured process. A history of direct trauma, ecchymosis and marked swelling are valuable when present, but often are absent. Backache, pain and stiffness in the back, weakness, muscle spasm and limitation in movements of the back usually are present in these fractures, but occur also in other injuries and diseases of the back, and

hence are of little value in differential diagnosis. Speed¹⁰ mentioned abdominal pain and rigidity and also localized pain on voluntarily raising the lower extremity while in a supine attitude. The latter test is positive also in diseases of the vertebral bodies and intervertebral joints and disks, and hence is of little differentiating value.

Before the use of roentgenograms, fractures of the transverse processes never were diagnosed clinically. Now they are not uncommon. Anteroposterior (preferably stereoscopic) and lateral roentgenograms should be taken in practically every case of alleged injury to the back. They determine definitely recent or old injury to the bone, disease of the bones or joints and congenital anomalies, and help to eliminate from consideration certain widely advertised "pinched nerves" and "vertebrae out of place" (a phantom of the laity which is assuming serious importance in some states in the management of conditions of the back). Recent fractures present sharply-defined, ragged, irregular surfaces in contradistinction to the smooth, curved surfaces with interposed joint space seen in accessory rudimentary ribs. Healing fractures show callus as early as the third week. Ununited fractures usually are recognized by the displacement or attitude and position of the fragments, and may resemble lumbar ribs. Roentgenograms taken at intervals often will clear up the diagnosis in questionable cases. Old healed fractures often are difficult to recognize.

PROGNOSIS

Uncomplicated by other bony injury, fractures of the transverse processes usually heal completely with recovery of normal function of the back. Bony union usually takes place except where wide displacement of the fragments has occurred. Surgical removal of a fragment has not been found necessary in this series.

TREATMENT

Physiologic rest, the duration to depend on the severity of the injury, followed by early progressive active and passive motion are indicated. External heat in any form is comforting and probably favors the healing process. The value of diathermy and other electrical modalities is questionable, especially during the early stages of healing. The deep location of the transverse processes of the vertebrae and the rapidity with which diathermy diffuses through the tissues and circulating mediums (blood and lymph) leave a doubt in one's mind as to its value. Sedative diathermy, of course, is contraindicated. Absolute immobilization such as by plaster jacket or back braces, is believed to be unnecessary and inadvisable. Partial immobilization such as by rest in bed, simple strapping with adhesive plaster or a properly fitted corset-belt, with the back in the normal erect attitude should be maintained until

few were without symptoms in the back when first seen. Several had been given the diagnosis of "back strain" and came under my observation because satisfactory progress had not been made.

The accidents responsible for the fractures were blows or crushing injuries in seventeen, or slightly more than half of the cases, while in fifteen cases the patients fell from heights of from 2 to 30 feet (61 to 914 cm.). In one case the history of the accident causing the injury to the back was overlooked by the examiner, who confined his examination solely to an injured lower extremity.

The attitude of the patient's body at the time that the injury was sustained could not be determined in ten cases. It was found to be one of flexion in seventeen, or in over half of the series, and of extension (erect posture) in only six cases. This is of interest when one con-

TABLE 2—*Relation of External Injury to the Mechanism of Fracture*

<i>Classification</i>	<i>Mechanism</i>	<i>No. Cases Per Cent</i>	
Local contusion, abrasion, swelling, ecchymosis or scarring	Direct	7	21.21
History, but no physical signs of trauma to the lumbar region	Probably direct	14	42.42
Trauma absent locally but present elsewhere (buttocks)	Indirect	2	6.06
History or physical signs of external trauma not recorded	Indeterminable	10	30.30
	Total	33	

siders the actual mechanism of the fractures, as illustrated in table 2. Attention is called to the fact that in only one third of the twenty-one cases of fracture resulting clearly from direct violence was there visible or palpable evidence, except for local tenderness, of injury to the soft tissues overlying the fractures. The absence of these signs is apt to lead the careless observer astray in his diagnosis. Only two of the thirty-three injuries were clearly the result of indirect muscular action. The regrettably high percentage of cases of indeterminable mechanism is due to inadequate histories and observations on the part of the examiners who first saw the patients.

Table 3 shows that the transverse processes of the first and fifth lumbar vertebrae, due to their protected positions, are least liable to injury. Those of the third vertebra were more frequently injured in the series studied. The right side showed a slight preponderance over the left in the actual number of processes fractured. That processes on both sides were fractured simultaneously in four cases suggests the mechanism of indirect muscular action in a higher percentage of cases than is evident from the figures in table 2. In one of these cases, how-

resorption of exudates has occurred and callous formation has begun. Passive and active motion should then be instituted and persisted in until a maximum return of function has been obtained. Light massage surrounding but not over the injured transverse processes aids both in resorption of hemorrhage and in healing. The therapeutic lamp is comforting to the patient and exerts a certain psychic effect.

OBSERVATIONS ON CASES

The present series consists of thirty-three cases of fracture of the transverse processes of the lumbar vertebrae occurring in a total of 42,634 hospital patients and outpatients, almost without exception industrially injured and sick. This is an incidence of one in every 1,430 patients. The ages of the patients studied varied between 18 and 64 years, the average being 37 years.

TABLE 1—*Occupational Incidence of Fracture of the Transverse Processes of the Lumbar Vertebrae*

Occupation	No. Cases	Per Cent
Laborers .	7	21.21
Truck drivers	7	21.21
Oil field workers	4	12.12
Carpenters	3	9.09
Ditch diggers	2	6.06
Plumbers .	2	6.06
Miscellaneous *	8	24.24
Total .	33	100.00

* Including one each of the following occupations: teamster, painter, dairymilkman, vulcanizer, electrician, shipping clerk, office manager and football player.

The occupational incidence is shown in table 1. That unskilled laborers head the list indicates merely that the same factors which make unskilled laborers of men also make them the most careless workmen and hence those most liable to injury. The equally high incidence in truck drivers emphasizes the increasing importance of automotive vehicles in industrial activities. Oil-derrick workers, carpenters and ditch diggers are unduly exposed to injury from falling objects or from falls.

The interval elapsing between the time of injury and the first observation of the patient varied from a few minutes to seventeen years. Ten patients were seen within twenty-four hours, nine within four weeks, eight within six months and six at various times in excess of six months after the original injury. In the cases in which the fractures were of long standing they were discovered during routine examinations for various related and unrelated complaints, a fact which emphasizes the importance of careful and complete examination of every patient. A

ever, a severe crushing blow fractured spinous and transverse processes of both sides and bodies of the vertebrae as well.

In the thirty-three cases studied there were twenty-two instances of associated injury to the bone. These included five fractured ribs, usually the twelfth, eight chip or compression fractures of the bodies of the lumbar vertebrae, two fractures of spinous processes and seven fractures of the pelvic bones, usually the ilium inclusive of one fracture of the coccyx. One case was complicated by traumatic spondylolisthesis. In thirteen cases, over one third of the total number, there were from slight to advanced hypertrophic changes on the bodies of the vertebrae

TABLE 3—*Relative Incidence of the Processes Fractured**

Vertebrae Involved	Total	Right	Left	Per Cent	
				Right	Left
I	2	2	0	2 66	
II	17	9	8	12 00	10 66
III	27	15	12	20 00	16 00
IV	31	13	8	17 33	10 66
V	8	4	4	5 33	5 33
Total	75	43	22	57 33	42 66

* Both sides were involved in four cases

TABLE 4—*The Relation of Displacement to Healing**

Status	Fractures	Per Cent	Displacement	Per Cent	No Displacement	Per Cent
Union	38	50 66	13	17 33	25	33 33
Nonunion	14	18 67	14	18 67		
Fracture too recent for healing	23	30 67	9	12 00	14	18 67
Total	75	100 00	36	48 00	39	52 00

* Gross malalignment was observed in two instances of healing

The aforementioned evidences of associated injury and disease are of interest only so far as they affected the period and extent of disability

Study of the roentgenograms disclosed interesting facts relative to the healing of these fractures as shown in table 4. In every one of the fourteen instances of nonunion, wide displacement of the separated fragment had occurred. Union had taken place, however, in 50 per cent of the fractured processes, even though displacement had occurred in approximately one third of these. In 30 per cent of the fractures, insufficient time had elapsed for healing to occur. The presence of bony union and nonunion in the same patient was observed repeatedly, ruling out constitutional deterrents to healing. In two instances healing occurred, although there was gross angulation of the separated processes.

DISABILITY

The disability is the primary consideration of the patient and, in these days of medical and surgical compensation of the employer and the insurance carrier as well. It is also the major interest of the physician, since it is the most accurate measure of functional recovery of the injured parts. Thomas,¹⁸ in seventeen uncomplicated cases of fractured transverse processes, reported a permanent disability of from 30 to 40 per cent, which seems high. Skillern¹⁹ found ablation of a fractured process and massive callus necessary for relief from pain after five months of disability, and noted immediate relief with return to work after two months.

In the present series of thirty-three cases the period of disability was greatly prolonged in nine patients who sustained associated fractures of bodies of the vertebrae, pelvic bones or bones of the extremities.

TABLE 5.—*The Average Number of Processes Fractured and the Period of Disability in Twenty-four Cases Without Other Injury to the Bone*

Period of Disability *	Age, Years	No of Cases	Average Number of Processes
0-1 month	18-60	5	1.8
1-2 months	20-55	5	2.0
2-3 months	22-64	6	2.3
4-6 months	31-44	4	2.5
6 months and over	30-39	4	2.25 †

* The minimum disability was 0 (3 cases) and the maximum disability 7 months (3 cases)

† Separation of the lumbar rib in one case

The few instances of permanent disability occurred in this group. In the remaining twenty-four cases of uncomplicated fracture of the transverse processes the temporary disability ranged from zero in three cases to slightly more than seven months in three other cases. The relation of age and the number of processes fractured to the period of disability is shown in table 5. In the patients with actual disability for less than one month the ages ran from 18 to 60 years, whereas in those disabled from six to seven and one-half months, the ages varied between 30 and 39 years. This indicates that age is a negligible factor in disability, at least in this series. The average age of the patients was 37 years. Two thirds of the patients are seen to have had a disability of less than three months, with the period from two to three months claiming slightly the larger number. It should be stated that the period of disability in every

18. Thomas, A.: Spinal Fractures, Colorado Med 25:19 (Jan.) 1928.

19. Skillern, P. G., Jr.: Ununited Fracture of Transverse Process of Fifth Lumbar Vertebra, with Massive Callus, S. Clin. North America 2:283 (Feb.) 1922.

case has been reckoned from the date of injury to the time when the patient actually returned to and was able to continue his regular work. In seven instances the patients were doing light forms of work for periods ranging from three weeks to five months prior to the actual discontinuation of temporary disability. In other words they had a partial disability, with compensation adjusted accordingly, until they were able to resume their regular work. The period of disability is seen to increase in approximately the same ratio as the number of processes fractured.

The effect on the period of temporary disability of factors other than the extent of the injuries is of both academic and practical interest. For example, one patient continued with his work for four weeks after his injury; then, on learning that he had sustained a fracture, he was disabled for the same type of work for a further period of four weeks

TABLE 6—*Disabilities in Twenty-four Patients with no Other Injury, Who Received Ambulatory Treatment and Were Allowed to Rest in Bed*

Type of Treatment	Duration of Treatment, Weeks	No. of Cases	Average No. of Processes Fractured	Average Disability, Weeks
Ambulatory	9	2.00	4.5
	{ Under 1	3	2.00	10.0
	{ 1 to 2	3	1.33	17.0
Rest in bed	{ 2 to 3	4	2.50	12.5
	{ 3 to 4	3	2.66	25.0
	{ 4 to 5	1	3.00	18.0
Undetermined		1*		

* No data in history.

Another patient alleged persisting disability in the absence of physical signs; at the end of four months he confided in the examiner to the extent of offering \$50 for a surgeon's report so executed as to secure a permanent indemnity for disability through a personal accident policy that he had carried for several years. When an attempt was made by the examiner to have this patient sign an agreement to that effect, his alleged disability immediately ceased and he has not been heard from since. Still another patient, who sustained his injury during a football game, finished the game and resumed his usual work the following day complaining only of a "sore back" for a few days. His fracture was discovered by the examiner several months later during an examination for a subsequent injury. Complicating osteo-arthritis was felt to have prolonged somewhat the period of temporary disability in a few cases.

In table 6 is given a comparison of the periods of disability in patients who had ambulatory treatment only and in those who had rest in bed for various periods preceding the ambulatory treatment. In the twenty-four uncomplicated cases of fracture of the transverse proc-

esses, nine, or slightly more than one third of the patients, were treated by the ambulatory method alone, that is, by partial immobilization, physiotherapy and relative rest of the muscles of the back. Their average temporary disability was four and one-half weeks, and the average number of processes fractured was two. Though not indicated in the table these fractures presented little or no displacement of fragments, a factor that I believe has a direct bearing on the rapidity of healing and, hence, on the duration of temporary disability. The patients requiring increasing periods of rest in bed show a relatively larger number of transverse processes fractured and a corresponding increase in the duration of temporary disability. In Kennedy's¹⁶ series of ten cases the period of hospitalization ranged from two to thirty-two days. In my fifteen patients with uncomplicated fractures who required hospitalization, the actual stay in the hospital varied from three to thirty-five days, the average period being seventeen days.

REPORTS OF CASES

CASE 1.—C. E. M., a pipe fitter, aged 50, sustained a crushing injury in the lumbosacral region in January, 1911. While he was on his hands and knees the corner of a two-story bunkhouse fell on him. He was immediately disabled, walked with crutches for five years and did no work for ten years. During the last six years he has worked steadily as a fitter. Roentgenograms (fig. 1) sixteen years later showed a fracture of all the transverse processes on the right side and of three on the left, fracture of the twelfth rib on the right and compression fracture of the body of the fifth lumbar vertebra. The fractured fragments were widely displaced (a maximum distance of 5 cm.) from the parent bones, except for those of the fourth and fifth transverse processes which had united. The distal end of the fractured twelfth rib lay in an inverted position in the soft tissues, 4 cm. below its parent bone. The prolonged disability in this case was due chiefly to the compression fracture of the body of the fifth lumbar vertebra. The case illustrates the point that surgical removal of ununited displaced fragments is not indicated unless they are causing symptoms of pressure.

CASE 2.—A. E. M., a carpenter, aged 38, on May 11, 1927, while stooping over, was struck in the left lumbar region by two falling scantlings. There was an abrasion contusion and exquisite tenderness over the left upper lumbar regions. Roentgenograms (fig. 2A) showed fracture of the left transverse processes of the second and third lumbar vertebrae with slight lateral displacement of the third. This patient still complained of aching pain in and stiffness of his back seven months after the injury, although x-ray pictures at four and a half months (fig. 2B) showed healing in good position.

CASE 3.—L. I. McG., an oil driller, aged 44, on Aug. 16, 1927, was struck in the left lumbar region by a timber, 2 inches by 8 inches by 12 feet (5 by 20 by 365 cm.), which toppled over from a vertical position. He was faint and felt immediate pain. He remained in bed at home for one week, and then consulted a physician who, after what must have been a very superficial examination, diagnosed the condition an "injury to the back" and prescribed physiotherapy. Massage

continued to be so painful after four weeks that x-ray pictures were taken (fig. 3A). They showed fracture of the left transverse processes of the third and fourth lumbar vertebrae with good callus and good position. At three months (fig. 3B) union was complete. The patient continued to complain of pain in the back and disability in the absence of substantiating physical signs. It developed that he was maliciously alleging disability in the hope that he might secure indemnity from a personal accident policy. Exposure of his attempt to bribe the

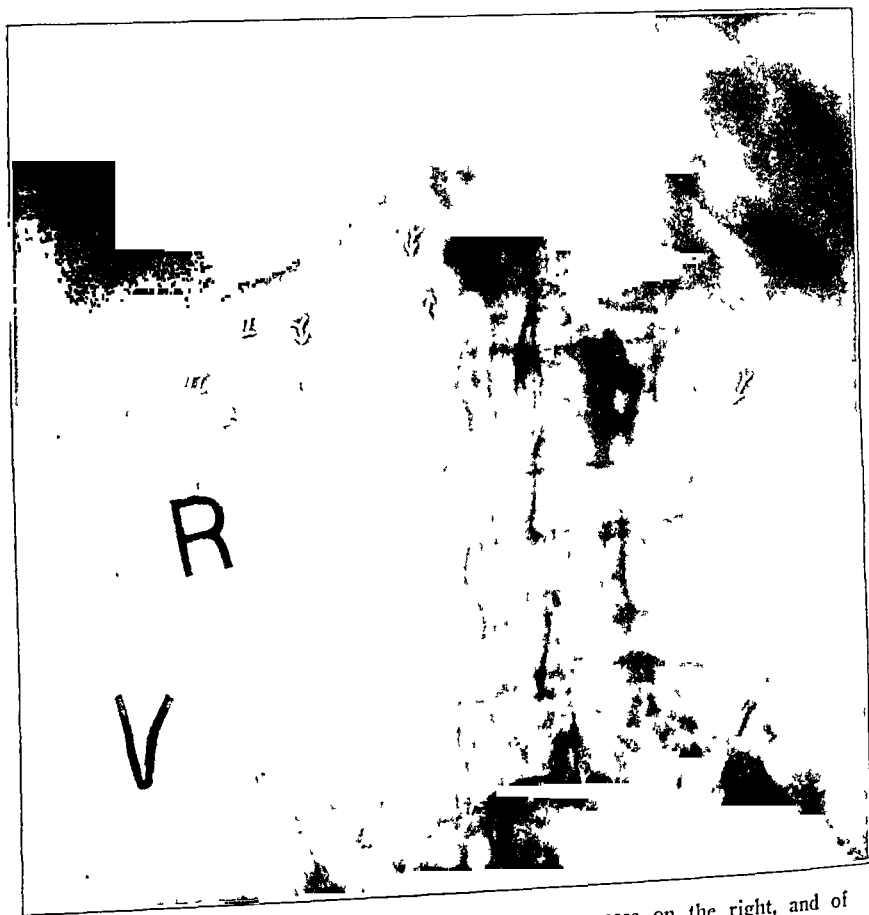


Fig. 1 (case 1).—Fracture of all transverse processes on the right, and of three on the left; fracture of the right twelfth rib and compression fracture of the body of the fifth lumbar vertebra

physician resulted in a sudden termination of his disability four months after the injury.

CASE 4.—This case illustrates an unquestionable instance of fracture by indirect violence (muscular action). H. M., a truck driver, aged 28, on March 10, 1928, was climbing into the back end of his truck when his foot slipped off the angle plate and he fell backward to the ground, alighting in a sitting posture on his right

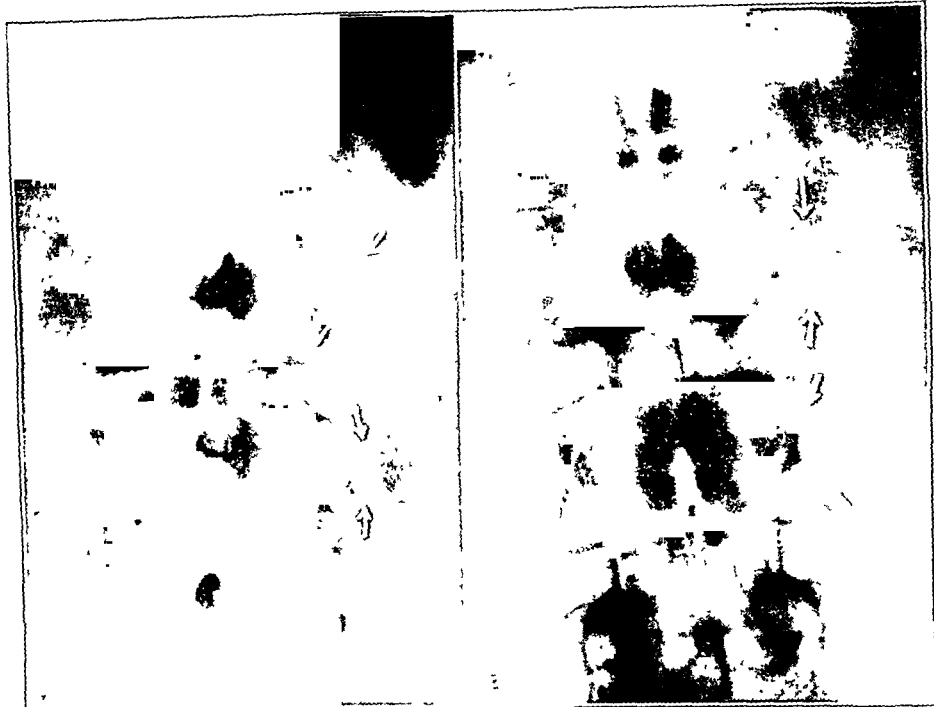


Fig. 2 (case 2).—*A*, fracture of the left transverse processes of the second and third lumbar vertebrae, with slight lateral displacement of the third; *B*, appearance of fractures four and a half months later, showing healing in good position.

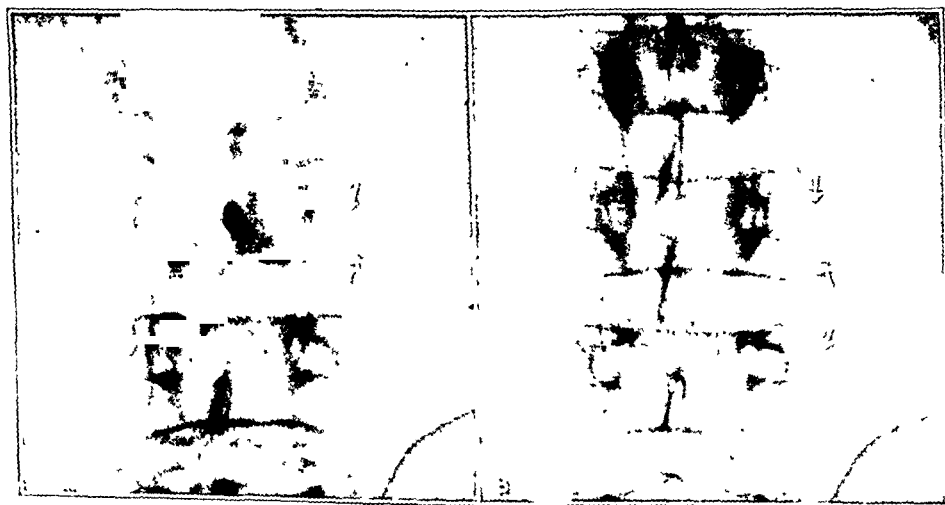


Fig. 3 (case 3).—*A*, fracture of the left transverse processes of the third and fourth lumbar vertebrae, with good callus and good position, four weeks after injury occurred; *B*, complete union after three months.

buttock. He stated definitely that he did not strike his back on anything. On regaining his feet and straightening up, he had pain in the lumbar region and in the right hip. He continued his deliveries, but with every second step experienced "sharp catch-like pains" in the right lumbar region; these became so severe after an hour or two that he could scarcely walk. His physician diagnosed the condition as "a spained back" and applied adhesive strapping. The patient remained in bed for four days. When examined on the sixth day there was marked tenderness over the right midlumbar region, with moderate spasm of the right sacrospinalis muscles. Left lateral bending, torsion and forward bending were painful and restricted. There was no external sign of injury on the skin of the lumbar region,

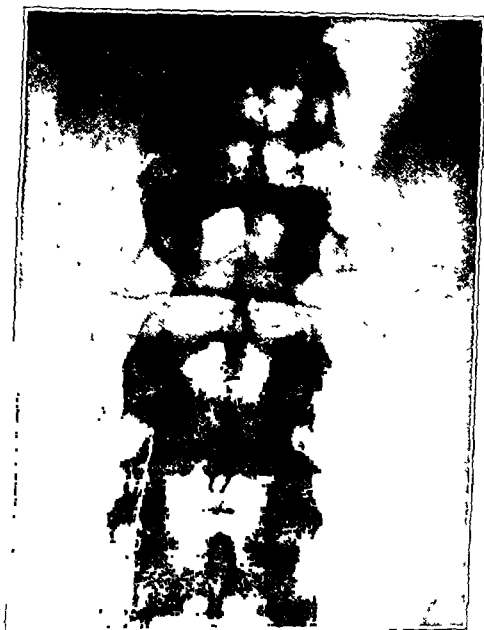


Fig. 4 (case 4).—Fracture of the right transverse process of the third lumbar vertebra due to muscular action.

but an area of tender cutaneous ecchymosis was found in the right gluteal fold. Roentgenograms (fig. 4) revealed a fracture of the right transverse process of the third lumbar vertebra. Temporary disability lasted for four weeks.

CASE 5.—A. L. G., a truck driver, aged 31, on March 12, 1928, while stooping, was struck in the right lumbar region by a 25 pound (11.3 Kg.) cast iron hoist weight. Pain and disability were noted immediately. For one day there were stinging shooting pains down the right thigh and leg, associated with numbness. Examination revealed an abrasion contusion in the right midlumbar region with tenderness in the lower lumbar region and spasm of the right sacropinalis muscles. Bending of the back was restricted and painful. Roentgenograms on the day of injury (fig. 5A) revealed fracture of the right transverse processes of the third, fourth and fifth lumbar vertebrae with a maximum lateral displacement of 1.5 cm.

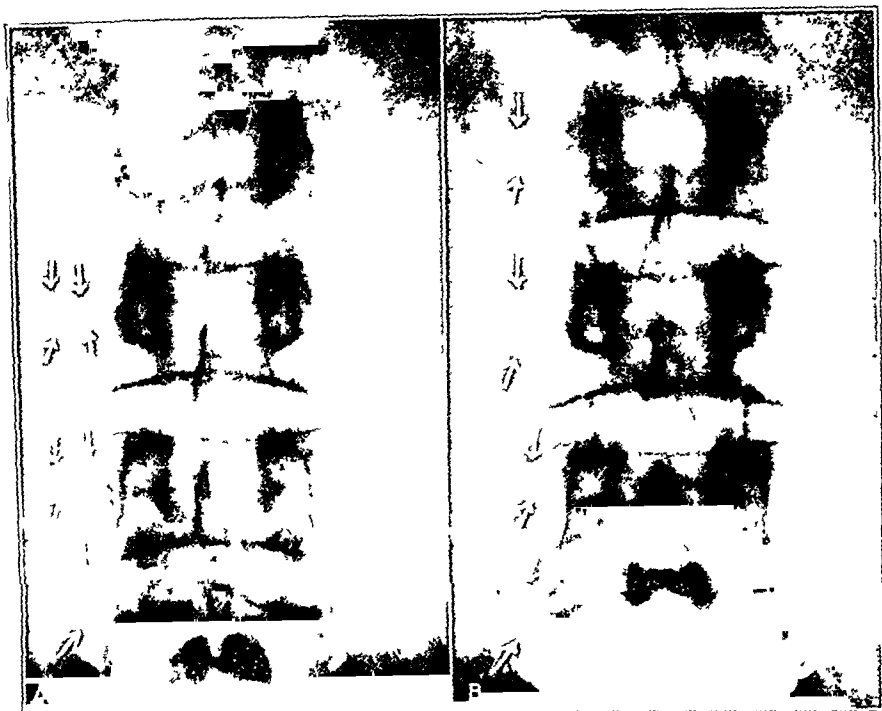


Fig. 5 (case 5).—*A*, fracture of the right transverse processes of the third, fourth and fifth lumbar vertebrae; *B*, appearance of the fractures at two months, showing union of the fifth process, good callus on the third, and nonunion of the fourth process with slight callus and displacement.

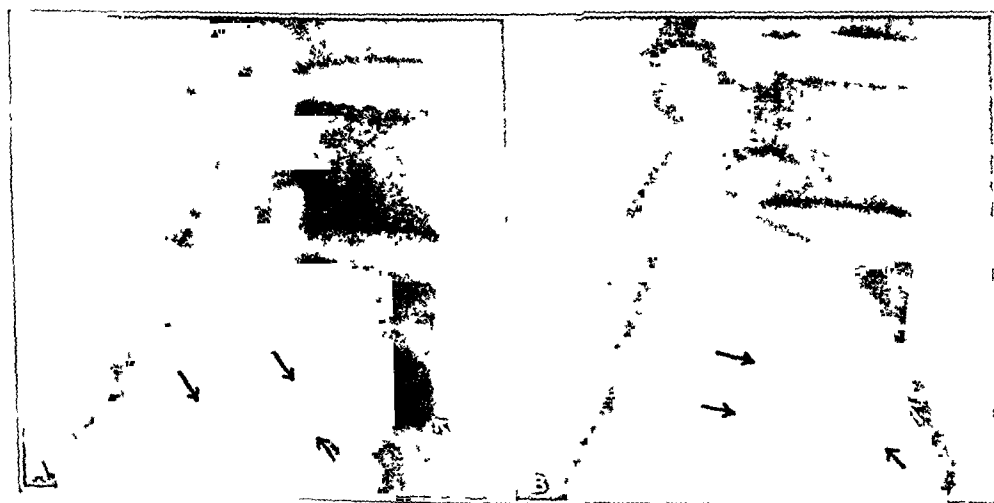


Fig 6 (case 6) —*A*, fracture of the articular processes of the fourth and fifth, with anterior displacement of the fourth lumbar vertebrae; *B*, complete reduction of the anterior dislocation.

of that of the fourth lumbar and a minimum displacement of 0.5 cm. of that of the fifth. Roentgenograms taken after two months (fig. 5B) showed union of the fifth process, good callus on the third and nonunion of the fourth process, with slight callus and displacement. This case illustrates the influence of displacement of the fractured fragment on the rapidity of the healing process.

CASE 6.—II. G., a Mexican laborer, aged 29, on Jan. 10, 1929, was struck on the right side and hip by a falling skip, causing him to fall across a ledge measuring 2 by 6 inches (5.1 by 15.2 cm.), where he was pinioned. Pain in the lower lumbar and right pelvic regions and loss of sensation and motor power in both

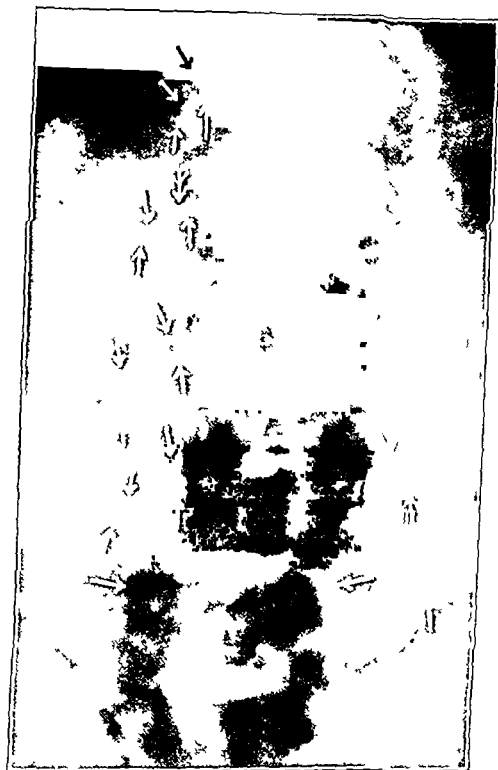


Fig. 7 (case 6).—Anteroposterior view, at the eighth week, showing little improvement in the lateral displacement.

lower extremities were immediate. Examination revealed severe contusion ecchymoses over the right hip, flank and lumbar regions with group paralysis and anesthesiae involving both lower extremities, especially the right. Voluntary control of both feet was lacking. Lateral roentgenograms (fig. 6A) taken on the day of the injury, showed fracture of the articular processes of the fourth and fifth with anterior displacement of the fourth lumbar vertebra equal to almost the diameter of its body. Under ether anesthesia, Dr. Herzikoff, who has permitted report of this case, was able to reduce the anterior dislocation completely (fig 6B).

although the lateral displacement was not materially improved, as is seen in the anteroposterior x-ray picture taken at the eighth week (fig. 7). This roentgenogram shows well the fractures of the right first, second, third and fourth and left third, fourth and fifth transverse processes, as well as the fractured articular processes. At the eleventh week the patient had regained almost normal sensation and moderate motor power in all muscles except those controlling the right foot.

The following case illustrates fracture of the transverse processes by muscular action.

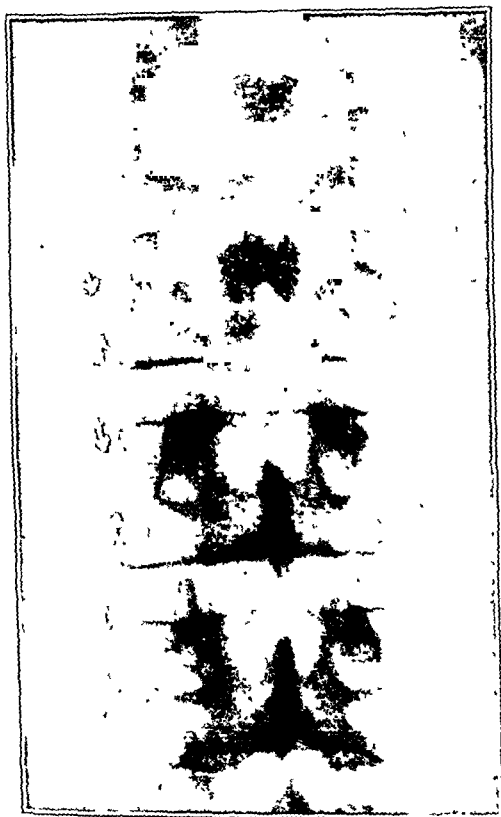


Fig. 8.—Anteroposterior view of oblique fractures of the right, second, third and fourth transverse processes and fracture of the right eleventh rib, at its angle

CASE 7.—G. B. Q., white, an electrician, aged 34, on April 8, 1929, fell backward eight feet (243 cm.), alighting on the right hip, scapular regions and head on a smooth concrete floor. He definitely stated that there were no projections or loose objects on the floor. He had immediate and persistent pain throughout the right lumbar and lower dorsal regions but no ecchymosis or other external signs of injury either then or during the ensuing days. An anteroposterior roentgenogram (fig. 8), taken three weeks after the accident, revealed oblique fractures of the right second, third and fourth transverse processes and fracture

of the right eleventh rib at its angle, with no definite evidence of callus. He was still in bed three weeks after the injury occurred and the area over the fractured bones was tender.

SUMMARY

1. The literature for the last fifteen years on fracture of the transverse processes of the lumbar vertebrae has been reviewed.

2. Most writers recognize that these fractures result from both direct external violence and indirect internal violence (muscular action); a few deny that these fractures can result from indirect violence.

3. Thirty-three cases are reported, in two of which fracture undoubtedly resulted from indirect muscular action. In 42 per cent of the cases of this series, fracture unquestionably was due to direct external violence.

4. The transverse processes of the second, third and fourth lumbar vertebrae constituted 85 per cent of the total number of fractures in this series. Fracture occurred bilaterally in the same patient in four instances.

5. The patient's body was in an attitude of acute flexion in slightly more than 50 per cent of the cases at the time that the fractures were sustained.

6. In nine (27 per cent) of the thirty-three cases, associated fractures of the pelvic bones, the bodies of the lumbar vertebrae or the ribs occurred. *Hypertrophic arthritis was present in thirteen (39 per cent) of the patients.*

7. Of the seventy-five instances of fracture of the transverse processes, nonunion resulted in fourteen (or 18 per cent). In every instance of nonunion, the fragments were widely displaced.

8. Temporary disability in the twenty-five cases uncomplicated by other fractures lasted, on the average, slightly more than ten weeks. The minimum period of disability was zero, and the maximum slightly more than seven months. None of these patients was permanently disabled and in none was resection of the fractured processes found to be necessary.

CONCLUSIONS

1. Fractures of the transverse processes of the lumbar vertebrae result from both direct external violence and indirect internal violence (muscular action).

2. Failure to appreciate this fact, to examine patients carefully and to take roentgenograms results in frequent error in diagnosis.

3. Nonunion usually is the result of displacement of the fractured fragments.

4. The duration of disability often is influenced as much by psychic and personality factors and by the provisions of state compensation laws as by the severity of the injury itself, as indicated by physical examination and roentgen observations.

GROSS AND MICROSCOPIC STRUCTURE OF THE THYROID GLAND IN MAN *

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Numerous investigations concerning the structure of the thyroid gland have been made in the past, but these, for the most part, have dealt with the morphology of the follicles, about which there still seems to be marked differences of opinion. It is my purpose in this report to present the results of a study of the normal human thyroid and also of the gland in cases of exophthalmic goiter from the standpoint not only of the individual follicles, but also of the structure of the gland as a whole and of the various subdivisions or units into which the thyroid is divided.

That the follicle of the thyroid represents the ultimate histologic unit of the gland is now conceded by all investigators, but in the intensity of the researches concerning the shape and size of these follicles and their discontinuity, its morphologic structure as a whole, and the manner in which this glandular mass is again subdivided into larger regions or areas composed of many follicles, has not been described. Heretofore, only very small areas of the gland have been studied by means of the wax plate reconstruction method, with the result that the morphology of only a few follicles has been determined. These investigations will be referred to later. In this study not only was the wax plate reconstruction used to investigate a larger area of thyroid tissue than had heretofore been reconstructed in wax, but the method of maceration and microdissection was also employed. By utilizing this larger area of the thyroid reconstructed by the wax plate method, I have been enabled to visualize the actual spatial relationship not only of the individual follicles, but also of the various regions, and to determine the presence or absence of a true lobulation of the gland. Reference was continually made to the stained sections during the process of transference to the wax plates of the tracings of the photographs made of them, in order that all epithelial elements would be included and the existence of interacinar cell rests, fetal or adult, might be determined. Serial sections of 10 and 20 microns, respectively, in thickness were studied for this purpose. No evidence of the presence of undifferentiated epithelium between the acini or

* Submitted for publication, May 13, 1929.

* From the Carnegie Institute of Washington, Department of Embryology, and the Department of Surgery, Johns Hopkins University.

follicles could be discovered in any of the sections. No epithelium, except that which is completely differentiated, and also which presents the arrangement of the normal parenchyma of the thyroid, exists in the adult gland. There is a great variation in the size of the individual follicles, and although there are in the normal gland many small ones in which a lumen is scarcely visible, nevertheless, from the histologic point of view, these smaller follicles are just as much and just as important a portion of the parenchyma of the gland as the larger follicles. It was evident, after examining the stained serial sections in conjunction with constant reference to the wax model, that small clusters of epithelial cells not arranged in acinar formation which apparently lay between various follicles, the latter having been cut in that particular section through their maximum diameter, were merely the beginning of other follicles situated in the gland and also in the model at different levels. A tangential section through the dome of a spheroid-shaped follicle or the end of a tubule-shaped one, which does not expose the lumen of the follicle, gives the impression of a group of interacinar cells which have not assumed the form and arrangement of an adult follicle or the remainder of the parenchyma of the thyroid. This, however, is an illusion and no evidence of any interfollicular fetal cell rests or clusters of differentiated epithelium, which were not a portion of the parenchyma, was demonstrable. The presence of many small follicles interspersed throughout the gland between the larger ones was also of interest. From the small size of the lumen in these follicles it might be suggested that they were probably not functioning to so great an extent, if at all, as the larger ones, and that they formed as it were a sort of a reserve supply. (Dr. Bensley¹ suggested that no gland functions equally throughout its entirety when stimulated, so that one should not expect all the follicles to be of the same size or to contain the same amount of colloid.) The noticeable reduction in number of these smaller follicles in the pathologic thyroid associated with exophthalmic goiter was striking and would seem to suggest that these small follicles of thyroid epithelium are capable of enlarging when called into action. The wax model demonstrated the diversity in size and the variability in shape of the inner margin of the epithelial lining of the follicles, and therefore, the internal form, with their relative position, but the structure of the gland as a whole, the morphology of the regions into which the gland is divided and the true external form of the follicles could be determined only from the dissected specimens.

Although larger areas of the normal human thyroid and the thyroid in exophthalmic goiter were reconstructed in wax than ever before

1. Personal communication to the author.

described, still the small block of gland sectioned was inadequate to determine the morphology of the gland as a whole, the structure of the various subdivisions or units into which the thyroid is divided and the true external form of the follicles. The wax reconstruction of the thyroid in exophthalmic goiter, as already stated, showed an enormous increase in the size of the follicles, and indentations in the models of these follicles bore witness to the papillomatous infoldings of the epithelium. However, the small follicles which have been observed, in stained sections of the gland in exophthalmic goiter, to have been situated in a position peripheral to that of the larger follicles were shown both by the wax plate reconstruction and more strikingly by the maceration and microdissection to be *entirely discontinuous* from the larger follicles. The small ones were distinct individual follicles and not, as has been suggested, pseudopodial outpouchings of the epithelial wall of the large follicle. The follicles, both large and small, have a smooth external epithelial wall. The only papillomatous or pseudopodial irregularities are those observed inside into the lumen of the follicle. The true external form of the follicle was brought out by the maceration and dissection technic, whereas the internal shape or cast of the inside of the follicle was shown better by the wax models. By employing maceration and microdissection, it was possible to demonstrate that the main mass of thyroid gland is divided and subdivided into many connecting or annectent bars, bands and plates of parenchyma, which in turn are composed of individual, discrete and discontinuous follicles. There are no distinct and true lobules in the thyroid, and it is incorrect to speak of it as a lobulated gland. These plates, bands and bars of parenchyma are separated by clefts and spaces normally filled with tissue of mesenchymal origin, such as blood vessels, connective tissue, lymphatics and nerves. They vary markedly in shape and size, the gland being irregularly broken up by the clefts and open spaces which form by their connections a fenestrated labyrinth in the gland mass. These bars, bands and plates are always connected one with another, and no isolated regions of parenchyma completely surrounded by connective tissue were observed. The presence of an area of parenchyma in a stained serial section which seemed to be completely surrounded and isolated by connective tissue was proved to be an illusion. Such an area was reconstructed in the exophthalmic gland and will be described later in this paper. The parenchyma on the anterolateral surface was disposed in rather flat platelike regions with, of course, connecting bars and branches of tissue associating these areas with contiguous parenchymatous areas of the inner zones of the gland. In general, the surfaces of these plates were convex and parallel to the surface of the lobe. The surface

and long diameter of the plates, annectent bars and bands were usually parallel to the long axis of the body, and therefore, to the greater axis of the entire lobe. The anastomosing system of clefts and open spaces, which were previously filled with mesenchyme, were also roughly parallel to the long axis of the lateral lobe. The follicles were discontinuous and individual structures not connecting with each other. The shapes vary from a perfect sphere to a long narrow tube with almost all conceivable types of intervening shapes. Their size ranged from 0.02 to 0.897 mm.

MATERIALS AND METHODS

In this study of the morphology of the normal thyroid and the gland in exophthalmic goiter, two methods were employed: (1) the wax plate reconstruction and (2) maceration and microdissection.

The normal thyroid tissue used in this study was obtained from the pathologic laboratory of the Johns Hopkins Hospital. The tissue was carefully chosen from ten young adults who had succumbed to maladies which would not have affected the thyroid gland, or to postoperative deaths and accidents. The localities in which the subject was born, raised and was living were taken into consideration so as to eliminate the possibility of a patient having resided in a goitrous district. All of these patients were inhabitants of parts of the state of Maryland situated at or very near sea level.

The thyroid glands from eight patients with exophthalmic goiter were obtained from persons operated on by me, so that the clinical history, physical signs, preoperative treatment, operative observations and handling of the thyroid tissue after operation were known at first hand. Hence there remains no doubt that the patients from whom the glands were removed were suffering from typical and extreme cases of primary exophthalmic goiter. In the case from which the wax reconstruction was made, and from which part of the dissection is also shown, no iodine had been used as a preoperative measure, and so far as could be ascertained no iodine or goiter remedies in any form had ever been given to the patient. The case was a clinically typical one of exophthalmic goiter with a basal metabolism rate of plus 92. There were vascular thrills and bruits at the poles. A preliminary partial lobectomy was performed to secure thyroid tissue from a typical case of exophthalmic goiter which had been histologically unaffected with iodine. After the preliminary partial lobectomy had been done, the patient was treated with a compound solution of iodine in the usual manner and a later subtotal bilateral lobectomy was followed by complete recovery. The tissue removed at the preliminary partial lobectomy was used for both the wax plate reconstruction and the dissection described and shown in this report. A comparison between the two reconstructions before and after the administration of iodine will be made in a later paper. In the remaining seven cases of exophthalmic goiter, iodine was given to the patient for the first time and only used over a very short period. The dosage was 10 minims (0.6 cc.) three times a day for ten days. With the exception of this, these patients had received no iodine before admission to the hospital. The average basal metabolism rate was slightly above plus 60.

A block 4 mm. square was cut from a normal thyroid gland and also out of the tissue removed from the thyroid in the case of exophthalmic goiter already mentioned, following their fixation in a diluted solution of formaldehyde U. S. P. (1:10) for several months. Each of these blocks was then dehydrated in 50,

60, 70, 80 and 95 per cent solutions of alcohol for twenty-four hours. They were then placed in absolute alcohol for twenty-four hours, changes being made to a new solution twice during that time. Following this, they were subjected to a solution of absolute alcohol and ether for another twenty-four hours. The blocks were then placed in 2, 6, 8, 10, 12 and 14 per cent solutions of celloidin for twenty-four hours each. They were then embedded on separate blocks and hardened in chloroform, after which they were kept in equal parts of 85 per cent alcohol and glycerin. Sections were cut of both blocks serially at a thickness of 20 microns, after which they were stained with hematoxylin and eosin. Other blocks 4 mm. square were similarly treated and cut serially in sections of 10 microns in thickness. The series of sections 20 microns in thickness, however, were used for the wax plate reconstructions described in this report, not only for the normal gland but also for that of the gland from the case of exophthalmic goiter. The stained sections were mounted serially on slides in groups of thirty sections to each slide. Five slides were used, totalling 150 sections. These slides were then photographed on Eastman's bromide paper, 11 by 14 inches (27.9 by 35.5 cm.), being projected at a magnification of 75 times. Many exposures were made, and finally the exposure which brought out the finest detail was found to be that of six seconds. The bromide plates were at once developed, dried and compared with the stained sections for microscopic detail. This checking of each bromide plate was made to guard against the possibility of losing some detail due to either the necessity of changing the exposure because of heavier or deeper staining of any given section or, on the other hand, to the freshness or staleness of the developing solutions. Sometimes insufficient washing would brown the bromide paper to such an extent that another exposure would have to be made to avoid losing some of the microscopic detail. The thickness of the section being 20 microns, times the linear magnification of 75, results in 1,500 microns, or 1.5 mm., which equals the desired thickness of a wax plate required to give the proper depth at a magnification of 75 times. Wax plates of the thickness of 1.5 mm. were then molded and cut 19.6 cm. square. These plates were cut accurately at right angles so that when piled one on the other they formed a perfect cube. As shown in figure 1, another geometrically accurate right angle was formed by strips of pasteboard held in place by thumb-tacks on a drawing board covered with smooth paper. The edge of the bromide plate, as shown, was set inside the pasteboard right angle and the edge of the section which corresponded to the exposed portion of the plate was made equidistant on two sides by means of a 1 cm. isinglass ruler. This eliminated the error of slight distortion due to the section being exposed somewhat unevenly as regards the edge of the bromide plate. The plate was then fastened down on the top of a piece of tracing paper which in turn lay on a 1.5 mm. wax plate. By the use of a right angle shown in figure 2, two straight lines were drawn across the board, later across the bromide plate, and were then traced on the wax beneath. These lines cut each other at right angles near the center of the plate and formed lines of orientation for the later stacking of the wax plates. Two small nails or pins were driven into the drawing board on these lines at the extremities of the orientation lines so that the right angle ruler could be replaced each time with accuracy. Each bromide plate and its underlying wax plate were so marked through the entire series of both the normal and the pathologic thyroid sections. After the lines of orientation on the bromide paper and the underlying wax plate had been marked, the inner margin of the epithelial lining of each follicle was traced with the utmost care and thus transferred by means of the carbon paper to the wax plate beneath.

All epithelial cells in groups or clusters were traced in a similar manner regardless of whether or not a lumen was present. If only a few cells were evident, merely a solid mark, proportionate in size, was made. In the tracings, the outlines of the larger bands of connective tissue were also made in order to bring out in the model the ramifying tendency of these bands. The figures shown are actual photographs of the method reduced 5.75 times, and it is evident that the definition of the follicles in an unreduced 11 by 14 film would be much greater. The tracing was done with a steel stilet ground to a very smooth and pointed tip, so that greater detail could be obtained. Constant reference to the original stained section was made in order to be certain of the presence of all epithelial structures. Owing to these precautions, no groups of epithelial cells were omitted because not only was the bromide paper film checked with the stained section under the microscope, but the tracing on the wax plate was also corrected by comparing it

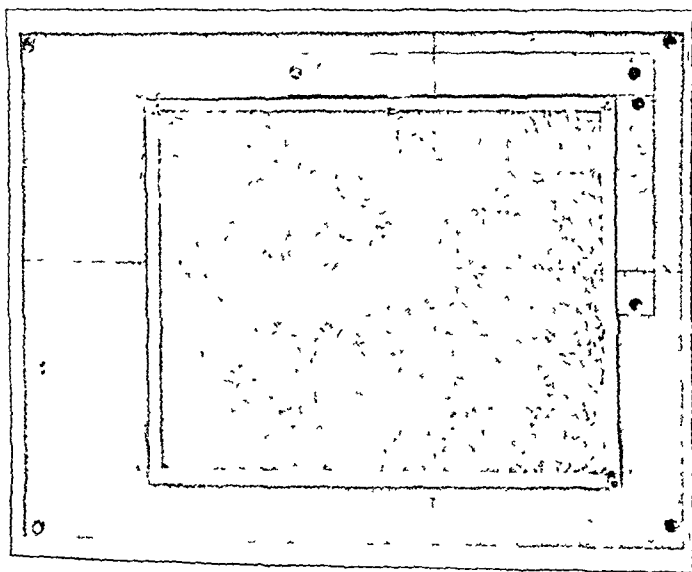


Fig 1—Photograph on bromide plate of a microscopic section from exophthalmic goiter. The wax plate is covered by carbon tracing paper placed beneath the bromide film. The drawing board with right angle pasteboard slips and orientation lines with guiding nails at their extremities is shown. An isinglass centimeter rule is placed between the exposed edge of the plate and the right angle pasteboard strips. Reduced to $\times 14$ from $\times 75$.

with the microscopic section, and in addition with the bromide film. The number of the slide, the row of the section and the number of the section in the row were photographed on the bromide paper at the time of exposure, by merely writing on the bromide plate with a pencil and then completing the exposure. The number was then traced on the wax plate. The entire microscopic detail of the bromide film was thus transferred to the wax plate. With a small knife the outline of the epithelial lining of the follicle was cut as shown in figure 3 for the normal and figures 4 and 5 for the exophthalmic gland. This was done by placing the wax plate on a square piece of plate glass. The knife would slide over the glass surface without engaging it. A burr, however, was formed on the upper surface

of the wax plate where the knife would split the traced line denoting the epithelial lining. A perpendicular cut was always attempted, to avoid the distortion of the positive model that would result from a slanting cut. The burr formation caused the wax to protrude slightly above the surface of the plate in general. The wax plate was then turned face down on the plate glass and a roller run over it, which exerted a certain amount of pressure on the entire plate, but more on the burrs which coincided with the carbon lines of the traced epithelial lining and the cut out portions. The glass plate having been carefully cleansed, it was immediately marked with the carbon lines outlining the follicles, and due to the wax burrs the cut out pieces became fastened to the glass so that the wax plate itself could be lifted away leaving the cut out portions adherent to the plate and in their correct position relative to one another. To meet these requirements the glass plate must be absolutely dry and cold. It will invariably happen that some

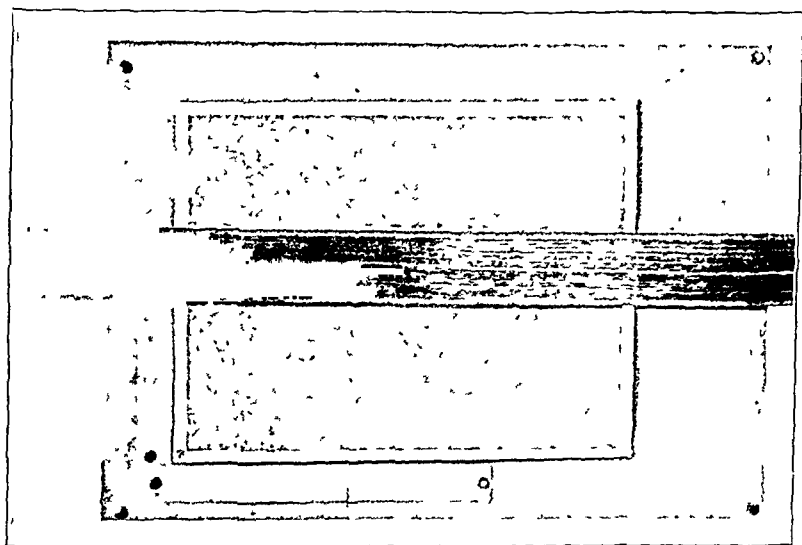


Fig 2—Right angle rule for drawing lines of orientation on a bromide film which also marks the wax plate beneath. The ruler is held in place not only by its right angle but as shown in the photograph by the nails at the extremities of the lines of orientation. Reduced to $\times 14$ from $\times 75$.

small pinpoint pieces of cut out wax, representing a few epithelial cells, will be moved out of place, but the mark on the glass where it originally impinged is usually sufficiently evident to replace the small piece accurately. In order that all cut out portions shall be absolutely true in their original position and especially with the relation to one another, the wax plate from which the pieces were removed is placed underneath the thin glass plate on which the cut out portions have become fastened, and these excised pieces are readjusted exactly over the area from which they have been cut out. They are firmly pressed down on the glass and then wired together by dropping a short piece of heated copper wire (no 2) over each piece (fig 6). If any pieces have been lost, displaced or remain undislodged in the plate, they can be detected readily and can be replaced by retracing one

follicle on a separate piece of wax. The network of disconnected pieces of wax wired together is then removed from the glass without distortion by passing a warmed spatula between the pieces and the glass. Again a comparison between the positive and the negative wax follicles can be made. The positive is then placed on marked cardboard squares to preserve its identity and prevent it from warping because of its weight. Each section was thus magnified 75 times and transferred to a positive wax plate formed by wiring the individual pieces together, and to a negative wax plate formed by cutting out the pieces representing the lumen of the follicle. These plates were then piled on one another by their orientation lines serving as a guide so that no axial distortion of the model might occur, and the exact spatial relation of the follicles was maintained. The size and shape of the inside of the follicles were shown. The course of the fibrous septums was also brought out. After the piling of the plates was finished, as many as possible

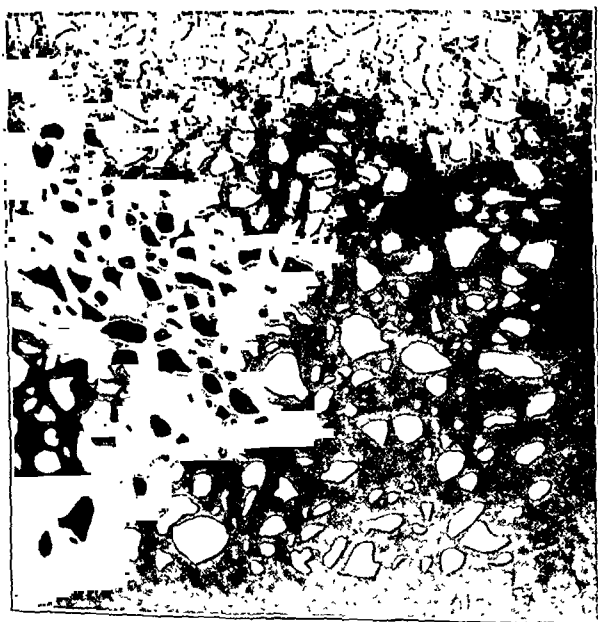


Fig. 3.—Negative wax plate of one section of the normal thyroid gland from which the inner lining of the traced epithelial follicles have been cut out. This area represents the group of follicles of one section of the series of microscopic sections the positives of which made up the wax model of the normal thyroid gland. The wax plate is 19.6 cm. square and 1.5 mm. thick. Reduced to $\times 18$ from $\times 75$.

of the wires were removed and the edges of the casts of the inside of the follicles were fused together and smoothed off with an electrically heated needle. The same technic was used in reconstructing the normal thyroid gland and the gland from the case of exophthalmic goiter. Photographs and drawings were made of the models before and after their completion (figs. 23 to 32).

As already mentioned, in order to study the morphology of the gland as a whole and the units or regions into which it is divided as well as the external form of the follicles, the method of maceration and microdissection was employed. Fresh glands, both normal and those from cases of exophthalmic goiter, were

placed in a macerating fluid which was first used by Siehler and later modified by Heuser.² That glandular epithelium becomes sharply delineated and connective tissue more transparent and swollen by acetic acid has long been known. The solution used by Siehler for macerating muscle and by Heuser² in his study of the uterine glands of the pig contained 5 per cent glacial acetic acid, 12 per cent glycerin, 1 per cent chloral hydrate and a diluted solution of formaldehyde U. S. P. (1 10), in an aqueous solution. This was employed in the present study. The thyroid tissue was fixed in this solution for three weeks, after which it was macerated for one hour at 60 C. in 5 per cent hydrochloric acid. The glandular epithelium would become white and opaque in the Siehler-Heuser² solution, while the connective tissue becomes swollen to two or three times its normal size, and more transparent. The consistence of the gland increases, so that the tissue is more firm and of greater stability for dissecting. The slight maceration in 5 per



Fig 4—Negative wax plate in which the inner lining of the follicles has been cut out. This area represents the group of follicles which were enclosed in the fibrous septums, constituting the area from which the wax model of the exophthalmic gland was made. About the periphery can be seen the outline denoting the inner lining of the follicles in adjacent regions of the gland which were not included within the fibrous septums chosen as the peripheral limit of the model. The wax plate is shown pinned down on the bromide film, superimposed on the photograph in order to be certain that all of the follicles have been cut out correctly and none overlooked. The wax plate is 19.6 cm square and 1.5 cm. thick. Reduced to $\times 14$ from $\times 75$.

2. Heuser, Chester H.: A Study of the Implantation of the Ovum of the Pig from the Stage of the Bilaminar Blastocyst to the Completion of the Fetal Membranes, Reprinted from *Contr. Embryol. Carnegie Inst. Washington* 19:229-243 (Aug.) 1927.

cent hydrochloric acid is just sufficient to soften the connective tissue encompassing the gland, thereby rendering subsequent dissection somewhat more easy.

The dissection of the thyroid was then carried out under the binocular dissecting microscope, with the tissue immersed in the Siehler-Heuser solution. The bottom of a glass dish 4 cm. deep and 11.5 cm. in diameter was covered with a layer of cork 1 cm. in thickness. The thyroid was placed in the dish and completely covered with the solution. It was then immobilized by means of silk tension threads drawn across its surface and fastened at each end in the cork by common pins. In this way the gland to be dissected could be held in any position for an indefinite length of time, the formaldehyde preventing decomposition of the tissue. The complete dissection of an entire right or left lobe and isthmus of a normal thyroid requires many months, not only because there is a great deal of work to be done, but also because one is not able to dissect for long at a time due to fatigue.

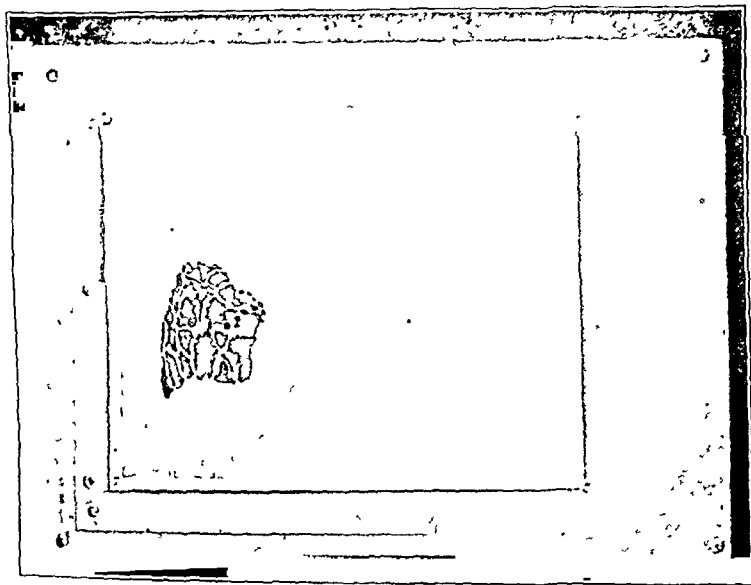


Fig. 5.—The group of follicles which have been removed from the wax plate shown in figure 4. This group has been wired together and superimposed on the corresponding bromide plate for corroboration of the position and grouping of the positive cast of the inner shape of the follicles for that section. Reduced to $\times 14$ from $\times 75$.

Somewhat to my surprise, a convenient differential staining reaction took place. As a result of the action of the iron pins, cork and Siehler-Heuser solution, the epithelial parenchyma of the thyroid became stained an opaque black gray, but the connective tissue and blood vessels were not affected and remained transparent and comparatively white. This facilitated the removal of the connective tissue and blood vessels because of the contrast in color, and also insured against the probable damage or removal of the parenchyma by dissection. This staining of the parenchyma was assumed to be due to the action of the tannic acid in the cork on the iron in the pins, as the Siehler-Heuser² solution alone did not seem to possess this quality. Sharp dissection was necessary because of the relative

firmness of the tissue, and to accomplish this, cataract knives of various shapes were ground down so that the blade of the knife was quite small. These were ground on a small (Arkansas) stone under the binocular low power, 55 mm. lens, which made it possible to minimize the serration of the edge of the blade. Needles and forceps were likewise ground down to as fine points as possible. Blunt dissection was of no avail after fixation in Siehler-Heuser² solution. A Spencer binocular microscope was used and for the entire lobe the 55 mm. lenses were found to give the optimal magnification, i. e., 44.4 times for dissection. Direct illumination from a 6 watt and 50 volt globe was used in an adjustable lamp. This could be focused and the light or beam concentrated, made more intense or more diffuse and thereby subdued, as desired. This flexibility of the beam was important because of difficulty in illuminating inaccessible areas or regions of the gland. A large amount of periglandular connective tissue was first dissected off the lobe and isthmus. This large amount of tissue was removed from the body with the gland in order to avoid injury to the thyroid. In the operative specimens as little damage to the gland was done as possible. Because of the differential staining, no difficulty was experienced in recognizing the smallest amount of parenchyma, even the thin edges of the platelike areas which seem to taper off into the connective tissue capsule. After the connective tissue and blood vessels (although they could not be recognized as such at this low magnification, it is presumed that nerve filaments and lymphatics were also components of this tissue which here is termed connective tissue) had been dissected away from the gland, large spaces and clefts remained which divided the parenchyma into many regions to be described later. In order to dissect into these crevasses and between and under these bars of parenchyma, resort was had to small radially arranged retracting silk threads fastened at one end by bent pin hooks into the parenchyma of the gland, and at the other by attachment to pins stuck in the cork. In this manner the parenchyma could be separated without damage by simply tightening up on the threads. Also the septums of connective tissue, which everywhere penetrated and divided the thyroid, could be followed and removed from the innermost regions and crevasses without breaking any of the connecting bands or bars of thyroid tissue. As the dissection progresses from the external surface of the gland to the interior it becomes increasingly difficult owing to the ramifications and the coral-like complexity of the gland which is more closely packed and interlaced in the deeper zones. The cleavage of the larger stalks and branches of connective tissue from the parenchyma is obtained with comparative ease, but dissection of the much finer strands of connective tissue binding together the individual follicles is far more difficult. The connective tissue septums of any considerable size are sufficiently macerated to render their dissection relatively much easier. By this method the morphologic structure of the thyroid as a whole can be demonstrated and the various regions into which it is divided can be identified. The tenacity of the interfollicular supporting tissue is illustrated by figure 7, which shows some of the fibers still clinging to individual follicles which were dissected away from a bar of thyroid tissue after maceration in 5 per cent hydrochloric acid only. These follicles were picked and plucked and rolled in petrolatum mixed with lampblack, but some of the connective tissue still remained adherent and could not be cleaned off. A portion of a fresh gland was macerated in 50 per cent hydrochloric acid for one hour at 60 C., but this procedure caused the follicles to break up completely, leaving only the colloid which was denuded of its epithelium. However, after fixation of the tissue for several weeks in a

diluted solution of formaldehyde U. S. P. (1:10), it can be macerated in 50 per cent hydrochloric acid for one hour at 60 C. and then the follicles may be dissected from the gland and each other with ease and contain the colloid within the epithelial sac. The thyroid tissue was transferred from 50 to 5 per cent hydrochloric acid for dissection. Very gentle dissection was imperative, especially with the thyroid tissue from the case of exophthalmic goiter, as the follicles are much more friable and more easily torn than the normal thyroid follicles. Porcupine quills held in fine glass tubes and the quill of the South American ant eater similarly held were found most efficacious as dissectors. Higher powered lenses were used than for the dissection of the entire gland. The tissue that was macerated and dissected for the study of the follicles was from the same gland that

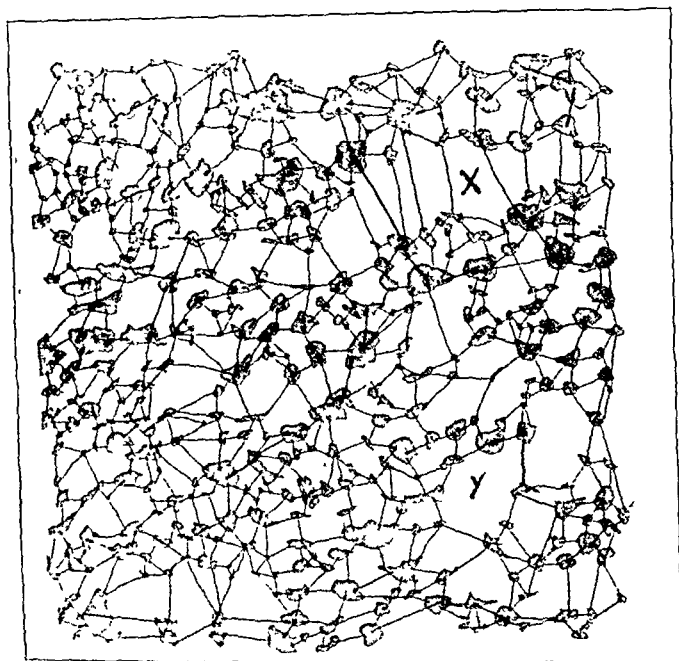


Fig. 6—The positive cast of a bromide plate of the follicles of one section of the normal thyroid gland after they were wired together. The preponderance of small follicles in proportion to larger ones is to be noted. The course of the fibrous septums can be seen at X in the upper portion of the photograph and at Y in the lower portion. These can also be traced later in a more complete model shown in figures 23 and 24. Reduced to $\times 21$ from $\times 75$.

was used in the wax reconstruction. The entire follicle with the colloid, epithelium and the follicular capillary bed was dissected out. The latter could be removed if desired. A portion of the epithelium was frequently cut away so that one might look down into the follicle and perceive the inside of this unit much as in a kaleidoscope. This was particularly true of the follicles from the cases of exophthalmic goiter. As the follicles were dissected free they were cleansed by removing all the adherent tags of connective tissue, sucked up into a pipet and placed in a group in a glass dish containing 5 per cent hydrochloric acid and in

the bottom of which was placed a piece of black glass. The dish was then completely filled with the 5 per cent hydrochloric acid solution and covered so as to exclude all the air in the dish and also keep out lint. The dish could then be moved about without disturbing the grouping of the follicles. Subdued direct illumination was used, and the groups were photographed. Individual follicles were held in position under the solution by placing them in a small ring of petrolatum which was placed in a hollow-ground slide before the fluid. In this manner, alternate sides of a follicle could be photographed. These specimens were also stabilized so that they could be handled by excluding all the air from the hollow-ground slide by means of placing a coverslip on the slide, a large ring of petro-

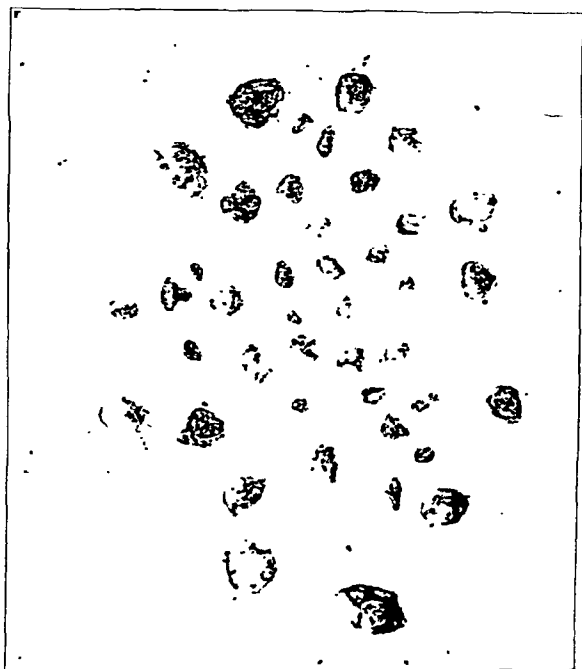


Fig. 7.—A group of follicles isolated by sharp dissection from a portion of the parenchyma of the normal thyroid gland after fixation in Siehler-Heuser solution for three weeks and maceration in 5 per cent hydrochloric acid at 60 C. for one hour. The follicles show tags of fibrous tissue which clung tenaciously. White areas in follicles represent portions of the wall composed by epithelium, which walls were thicker at that point than in the more clear areas where the walls were very thin and of the thickness of one epithelial cell only. The variation in size is typical of the normal gland, and the tendency for each follicle to be more or less spherical is also characteristic. The shiny colloid can be readily seen. Again the proportion of small follicles to large makes this a characteristic group for the normal thyroid gland; $\times 18$.

tum having been previously run around the edge of the hollow depression and the fluid brought up to the edge of the ring. Specimens can be preserved indefinitely in this manner.

DESCRIPTION OF DISSECTED GLANDS

As already mentioned, previous investigators of the structure of the thyroid gland have confined themselves to so large an extent to description of the individual follicles, that the morphology of the gland as a whole and the manner in which it is subdivided have been left undescribed. In this report the structure of the gland as a whole will first be described and illustrated; this will be followed by the morphology of the regions into which the gland is subdivided, and lastly, by a detailed account of the follicle or definitive unit of the gland. Thus an orderly sequence is adhered to which reveals the entire

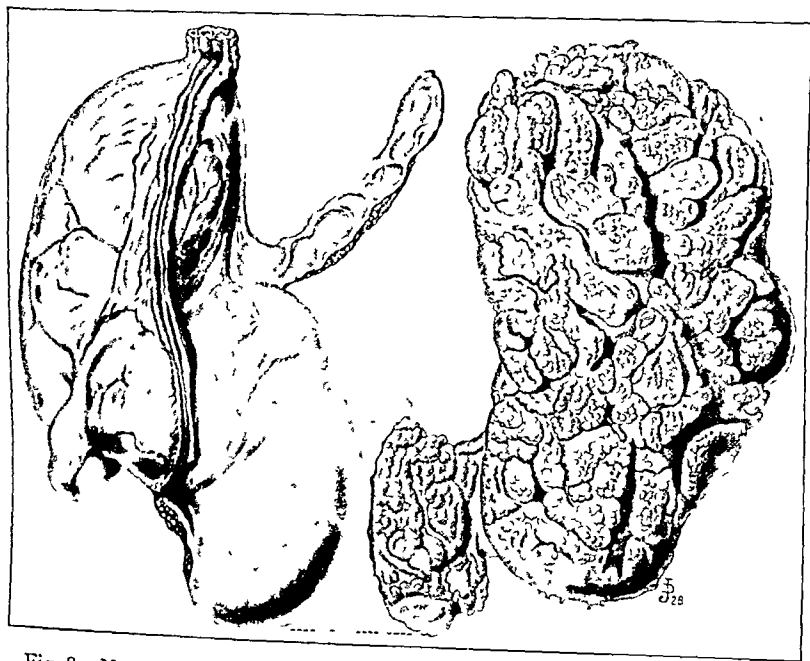


Fig. 8—Normal human thyroid, right and left lobes together with the isthmus. The dotted line shows where the isthmus, which in the section was left attached to the left lobe, joins the base of the right lobe. The right lobe is shown covered with fascia as it was found in the cadaver. The anterior branch of the superior thyroid vessels is seen descending from the upper toward the lower pole. From the junction of the upper portion of the right lobe can be seen a bizarre pyramidal lobe. The isthmus and the left lobe are shown with all fibrous tissue investment, including blood vessels, nerves and lymphatics dissected away. It is to be noted that there are no true lobules but a complex mass of parenchyma irregularly divided by an intricate anastomosing system of spaces or channels forming within the gland a veritable fenestrated labyrinth. The gland as shown is made up of regions of connecting bars, bands or platelike regions composed of individual discrete follicles or acini. The stippled appearance of the surface represents the follicles; $\times 1.4$.

structure of the thyroid gland. The normal gland and the gland in exophthalmic goiter are described and compared.

General Form and Subdivision of the Gland.—By employment of special fixation, maceration and microdissection, the connective tissue including blood vessels, nerves and lymphatics was dissected away from the entire left lobe and isthmus of a normal thyroid gland. In figure 8, the undissected right lobe of the same gland is shown for comparison. When the connective tissue investing the thyroid is removed with the blood vessels, lymphatics and nerves, the gland is revealed as a complex mass of tissue which is divided and irregularly broken up into many regions or areas of parenchyma.

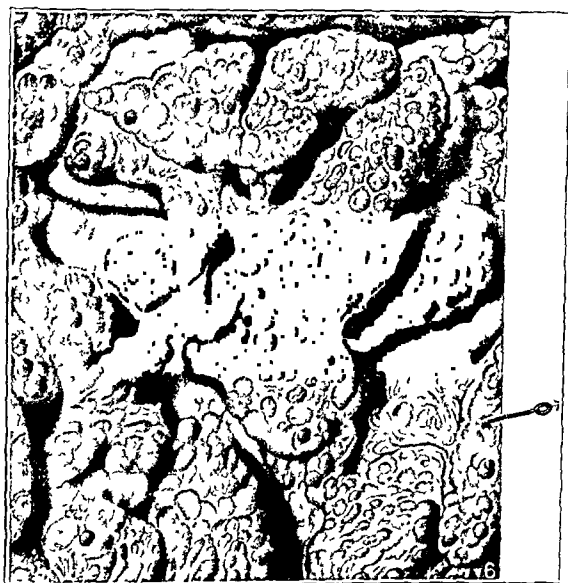


Fig. 9.—Normal human thyroid Higher magnification of the anterior superior portion of the left lobe is shown in figure 8. Note the small hook to the right of the drawing which demonstrates the pin retractor used for separating crevasses of the gland The various shapes of the parenchymatous regions are evident, varying from a triangular quadrangular area to that of a cube or almost perfect sphere Reduced from a magnification of $\times 12$

These areas or regions of thyroid tissue are in turn made up of groups of follicles of different number, shapes and sizes depending on the shape, size and location of the region which these follicles compose. The form of these regions varies widely and is inconstant Not only in the specimen depicted here, but also in other normal glands dissected this irregularity in form and size was noted. There seemed to be a total lack of uniformity not only between the various

subdivisions or regions of the same gland and lobes of the same gland, but also between various glands as portrayed by the different patterns shown on their surfaces. These regions or areas of the parenchyma of the thyroid may best be described as connecting or annectent bars, bands or platelike pieces of tissue. The entire lobe of the thyroid is irregularly traversed by septums of connective tissue carrying the blood vessels, nerves and lymphatics. In this manner the parenchyma is divided and subdivided into many regions which, as previously stated, have the greatest diversity in shape and size with but one constant feature; namely, that all these regions were joined to each other at one or more points and in no case was a portion of parenchyma so completely surrounded by connective tissue that it was isolated from

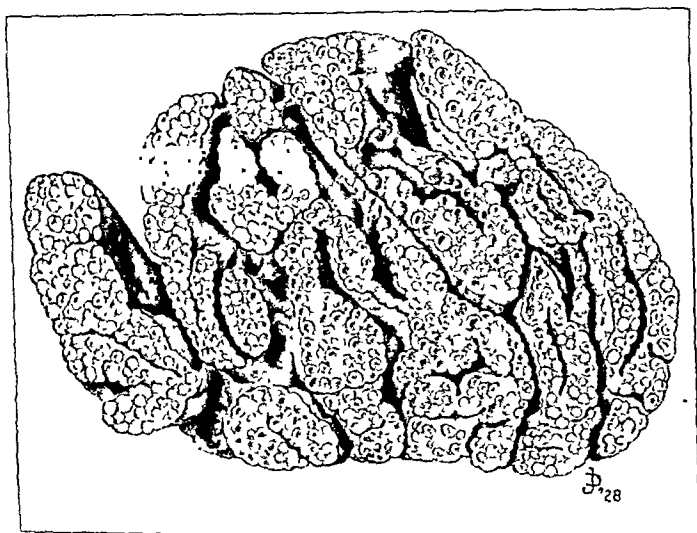


Fig. 10.—Cross-section of normal human thyroid. Cross-section of the superior anterior region of the dissected left lobe shown in figure 8 demonstrates anastomosing channels or spaces forming labyrinth. It is to be noted that clefts do not completely traverse the gland; $\times 2.5$.

the remainder of the gland. In some instances the annectent bar or connecting band of tissue between one region and another was only a small thin stem of parenchyma composed of a single row of follicles and their interfollicular supporting tissue, while in others the connecting stalk would be much larger in all dimensions and would approximate in size the regions which it joined together. After removal of the bands of connective tissue by dissection, the crevasses and spaces between the various regions of parenchyma extended throughout the entire lobe, forming a complex system of anastomosing channels ramifying throughout the gland and causing it to be broken

up and divided in an irregular manner, so that it formed a fenestrated labyrinth within the gland. The complexity and compactness of the coral-like arrangement of the parenchyma increased as the dissection was carried from the outside toward and into the inner zones. Unless great care is exercised in removing the outermost layers of connective tissue, a portion of the parenchyma may inadvertently be removed, for the relatively smooth convex surface of the thyroid is formed by broad, flattened, platelike areas of parenchyma which overlap each other much as do the feathers of a bird. The edges of these overlapping regions are thin, usually of the thickness of only one follicle. Probably as a result of the pressure of the contiguous structures in the neck, many of the surface regions of parenchyma become flattened and spread out with their connecting stalks or bars beneath the surface, giving the entire platelike region, in profile, the appearance of a mushroom or a palm leaf (figs. 9 and 10). The external flattening pressure is also reflected in the shape of the individual follicles which form the delicate overlapping edge, in that they are much thinner and more flattened than the follicles elsewhere in the gland. These tongues or edges of the flattened platelike regions of tissue forming the surface of the gland gradually blend with the connective tissue which invests the gland and become more attenuated until the plate ends by tapering off to a delicate point or nose composed of only a few follicles in a strand of connective tissue. Again, on the surface at the point of ingress or egress of the blood vessels, the delicate and prolonged end of a plate may be observed to have embraced the vessels and to be extending along their course for a short distance. Not all the areas of parenchyma presenting on and composing the surface of the gland are of the flat platelike variety, however, for some are distinct bars and bands in form, while others are spheroidal (fig. 9). There are all manner of gradations between these varieties of bands or bars and the spheroidal types of parenchymatous regions with no suggestion of uniformity. This point is well shown in figure 9. From this it can be seen that there are plates of parenchyma which on the surface appear triangular; others almost quadrangular, and others, again, almost perfect spheres. They are, of course, made up of a group of closely connected follicles, and all are connected with each other by some bridge, bar, band or fenestrated arm of thyroid tissue. In figure 9 an area is shown which is almost completely isolated from the surrounding parenchyma except for a narrow arm of tissue connecting the gland. If a section 10 microns in thickness had been cut through this spherical knob of the parenchyma of the gland either in a plane perpendicular to the gland or in one horizontal above the connecting arm, the false impression of a lobule of thyroid tissue completely surrounded by con-

nective tissue septums would have been obtained. The flattening of the surface plates is also well shown in figure 9.

The stippled appearance in figures 8 and 9 is caused by the follicles composing these areas of parenchyma. The higher magnification of figure 9 demonstrates this point more clearly. The open spaces or clefts often extend almost entirely through the lobe but are eventually

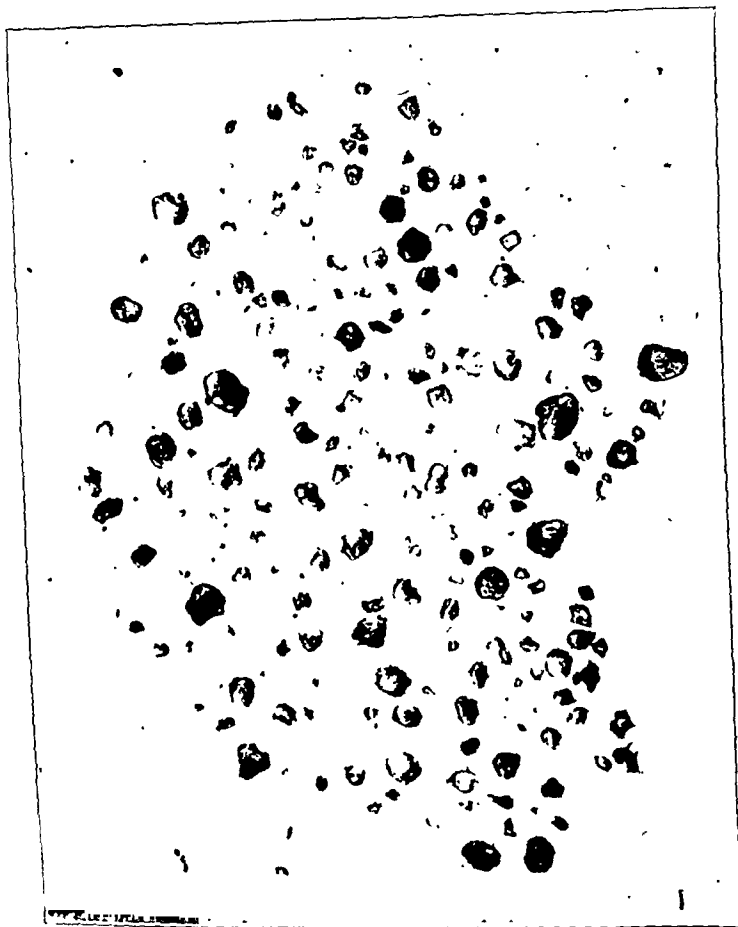


Fig. 11.—Photograph of group of follicles dissected from a normal human thyroid. Note the variation in size, also the marked transparency of some of the very small follicles. Compare with the more dense ones shown in figures 16, 17 and 18 which were dissected from the exophthalmic goiter. It is to be noted that the latter are much more white and dense due to the increase in amount of epithelium in proportion to the amount of colloid. The normal follicles are relatively spherical in shape with a smooth external contour. The white areas in the walls of the follicles are those in which the epithelium seems more thick and dense; $\times 67$.

made to end blindly by connecting bands or bars which join one portion of the gland with another. Figure 10 is a drawing of a cross-section of the lobe shown in figures 8 and 9, and brings out clearly the tendency of the surface parenchyma to take the form of a flat, platelike structure with two more or less flat surfaces and an edge. The larger number of annectent or connecting bars and bands or stalks of parenchyma joining larger regions of the inner zone together is to be observed in figure 10.

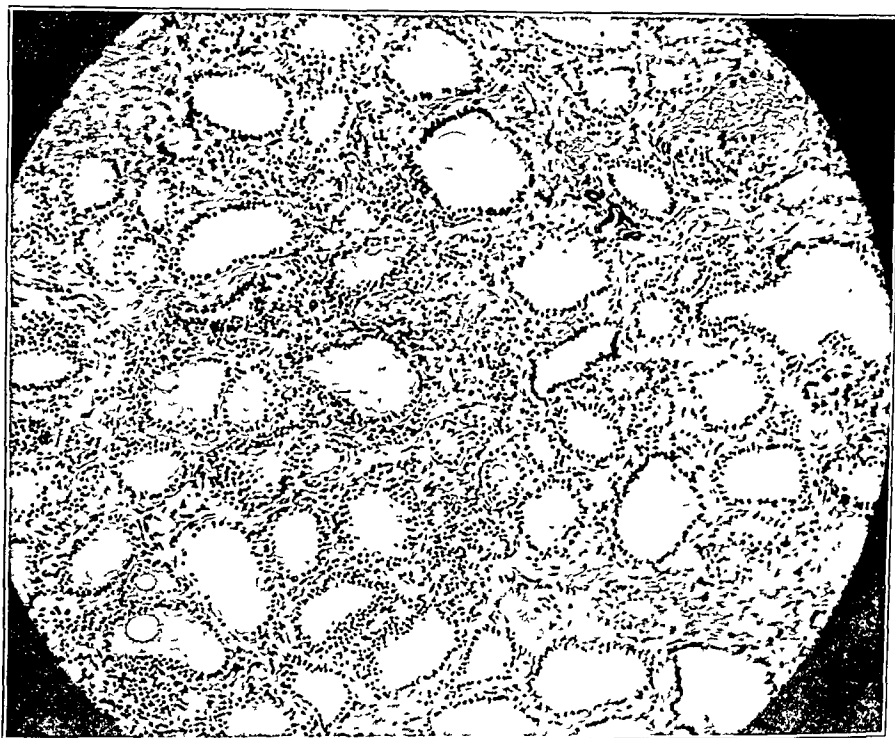


Fig 12—Microscopic section of normal human thyroid gland stained with hematoxylin and eosin. The follicles were dissected and the wax model made from same gland from which this section was removed. It is to be noted in this section that some follicles are cut through at their maximum diameter, while others are cut through at their minimum diameter. Some groups of cells shown between the larger follicles represent a tangential section through the dome of an underlying follicle. Thus, in any one section all the follicles are cut through at different levels, thus causing their diameters in a certain section to be entirely different. Follicles cut through their domes, so that the lumen of the follicle is not shown, give the impression of a group of interfollicular or inter-acinar cell rests; $\times 40$

As one progresses to the inner zones of the gland, the connective tissue septums are dissected away with a good cleavage from the parenchyma, leaving clefts and open spaces which twist and turn and penetrate the gland in all directions.

As mentioned before, the inner zone of the gland was more compact as well as complex than the outer zone. The parenchymatous

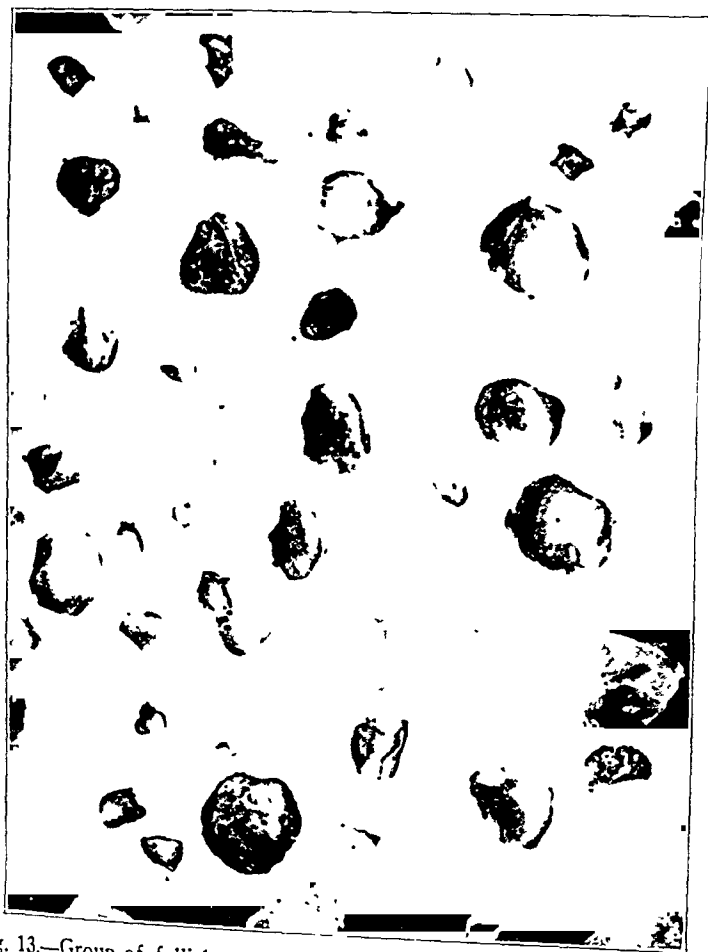


Fig. 13.—Group of follicles dissected from normal human thyroid. Spherical shape together with the variability and thickness of the epithelial wall as evidenced by the difference in the photographic shadow cast is well brought out. Points called attention to in legend of figure 11 are well shown in this figure; $\times 20.1$.

tissue seems to occur less in the form of the flat plates seen on the surfaces, but more in the nature of large columns or trunks and bars. Again, this difference in shape of the larger regions of parenchyma was reflected in the forms of the individual follicles which will be described later. Also the connecting links between the areas of gland-

ular substances were much greater in breadth and thickness and perhaps better described as bands rather than bars. In the glands observed in this study there seemed to be a definite stratification to the thyroid. This was manifested chiefly by the tendency of the plates, bands and bars of parenchyma as well as the open spaces and clefts to be roughly parallel to the long axis of the body and the surface of the gland. This tendency toward a stratification is not present or reflected in the follicles. No uniform and distinct lobules were observed, and further, no areas of parenchyma completely surrounded by connective tissue occurred. The foregoing description of the maceration and microdissection of the normal thyroid applies also to the gland as a whole in exophthalmic goiter, except that the exophthalmic gland with the various subdivisions is larger.



Fig. 14.—Anterior view of follicles dissected from normal human thyroid including the surrounding capillary bed, showing the vessel of ingress and capillary distribution. The white arc about the periphery of the follicle is due to the reflection of the light shown down on the follicles by the convex edge of the epithelial wall; $\times 85$.

The Individual Follicles.—The method of maceration and microdissection was particularly applicable to the study of the individual follicles of the thyroid in even a greater degree than to the morphology of the gland as a whole. By macerating the glands, after fixation in a diluted solution of formaldehyde U. S. P. (1:10), with 50 per cent hydrochloric acid, it was possible to dissect the most delicate follicular irregularities and the entire follicle with their anastomosing capillary bed without injury to either. The use of the quill of the porcupine and South American ant eater made possible the delicate separation

of the follicles from each other by perfect cleavage. The slightest tearing of these epithelial sacs was at once evident, and by dissecting so as to leave in situ the capillary bed, one could be sure that the wall of the follicle remained undamaged. The capillary plexus might then be removed, leaving the epithelial sac alone and intact. Furthermore, a break in the continuity of the epithelium allowed one to look down into the follicle, whereupon the torn epithelial edge could readily be seen and also the inner lining of the epithelial wall. The external form of the individual follicles was determined in this manner. The sources of error which are attendant on a wax reconstruction were eliminated by this method of investigation. In the studies of the individual follicles by previous investigators, and also, as will be pointed

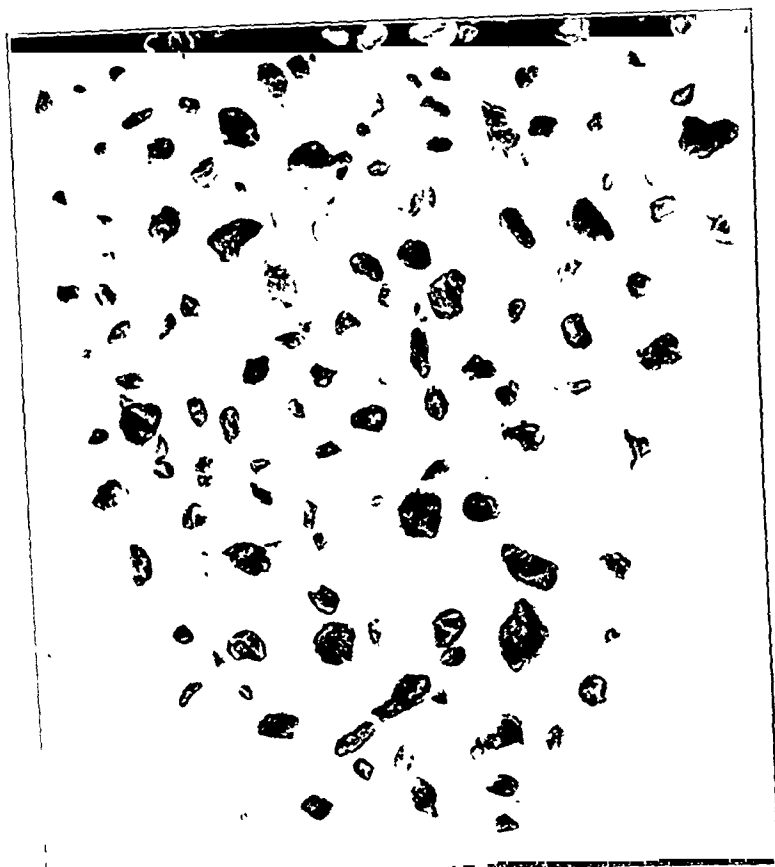


Fig. 15.—Posterior view of the same follicles shown in figure 14 to demonstrate the complete enclosure of the follicles within the capillary bed; $\times 85$.

out later, in the present study, as far as the wax models were concerned, the inner margin of the epithelial lining of the follicle has been used as a criterion of the shape of the follicle. This resulted from the fact that the inner epithelial margin of the thyroid follicle is more easily defined microscopically and traced than the external margin. The latter is not infrequently difficult to recognize in stained sections and therefore does not readily lend itself to an accurate tracing onto the wax. The resulting model is a cast of the inside of the follicle and portrays the internal form, whereas the follicle dissected entirely free from its surroundings after maceration reveals its true and actual shape, size and external form. Figure 11 shows a group of follicles which have been dissected from a macerated specimen of a

portion of the normal adult thyroid gland, also from which the wax reconstruction was made. The dissection was made under the binocular microscope at a magnification of 20 times and photographed in a subdued light at a magnification of 40 times. The stained microscopic section of this gland is given in figure 12. A great many of these follicles were so small and transparent that they faded out in the negative. However, faint traces of some of them may still be seen which appear to be mere fragments of follicles in the photograph. The subdued light was shown directly on the specimen at the time of photographing. The high lights in the follicles shown are the areas in which the epithelium was more dense or thick. This density or thickness in the epithelium seemed to be due to slight infolding of the epithelial wall and also to an increase in the size of the individual cells. In the less dense regions of the follicle wall there was just a thin layer of flattened endothelial-shaped epithelial cells in which no infolding of the epithelial lining existed. The more transparent areas in the follicles represent, therefore, regions in which the walls of the epithelial sac are more thin and translucent. The follicles are full of colloid which transmits light readily and therefore does not show up well in the photograph, thus giving the follicle the appearance of a closed epithelial sac containing a clear substance which maintains the normal contour of the follicular unit. The follicle is a structure in which the epithelial walls encircle a colloid substance contained within so that when direct light is shown on this unit the margin appears in the photograph to be of greater density and the follicle is therefore more plainly defined or outlined. The more clear areas of the follicles shown in the photograph are the regions in which there is a thin sheet of epithelium of only one flattened endothelial-like cell in thickness enclosing the colloid substance. In some follicles, especially the smaller ones, the entire epithelial sac is composed of the most thinned out epithelial sheet in which there is no infolding of the epithelial wall or even an enlargement of the epithelial cells. In the photograph these transparent small follicles hardly cast enough of a shadow to be photographed and they therefore are not all shown. As seen in figures 11 and 13 there is a great diversity in the size of the follicles, but the outstanding characteristic of the normal thyroid gland, as will also be shown in the wax model, is the great preponderance of the small follicles over the larger ones. The normal follicles vary from 20 microns to 1 mm. in diameter, but relatively only a few attain a large size. the great majority are small and in many there was hardly a lumen. There did not seem to be any special distribution of the follicles in regard to size. The larger ones were evenly distributed throughout the gland with the smaller ones.

The shape of these units varied as much as did the size. There were no two follicles alike. The smaller ones more frequently approximated to a true sphere than the larger ones. However, they were all spheroidal, i. e., a solid body with the points in the circumference about equally distant from the center of the body. The epithelial walls in each follicle encircled the colloid substance and there were all forms and shapes from that of a perfect sphere going through all stages of



Figs. 16, 17 and 18.—Dissection of group of follicles from gland of a patient with exophthalmic goiter. Figures 16 and 17 are from the same gland from which the wax model was made, while figure 18 is from another gland. Note the variation in shape and size of the follicle, also the increased definition and density of the follicles due to the proportion of increase in epithelium to the colloid. The magnification of each illustration is $\times 6.7$.

globular, oblong, triangular, cuboidal, hexagonal, octagonal, to that of almost a perfect cube. Some follicles were slightly faceted from pressure and others the least bit cupped on one surface because of resting on the dome of an underlying follicle, but on the whole the general form tended to be that of spheroidal with a tendency of the

follicle wall to be tapered off to a point at two or more areas, usually rather remotely situated on the follicle. The outside wall of the epithelial sac except for the facets, cupping or gentle tapering was essentially smooth. There were no pseudopodial outpouchings of the wall, nor regions showing constriction or budding of a primary into a secondary follicle. All the major irregularities in the epithelial wall

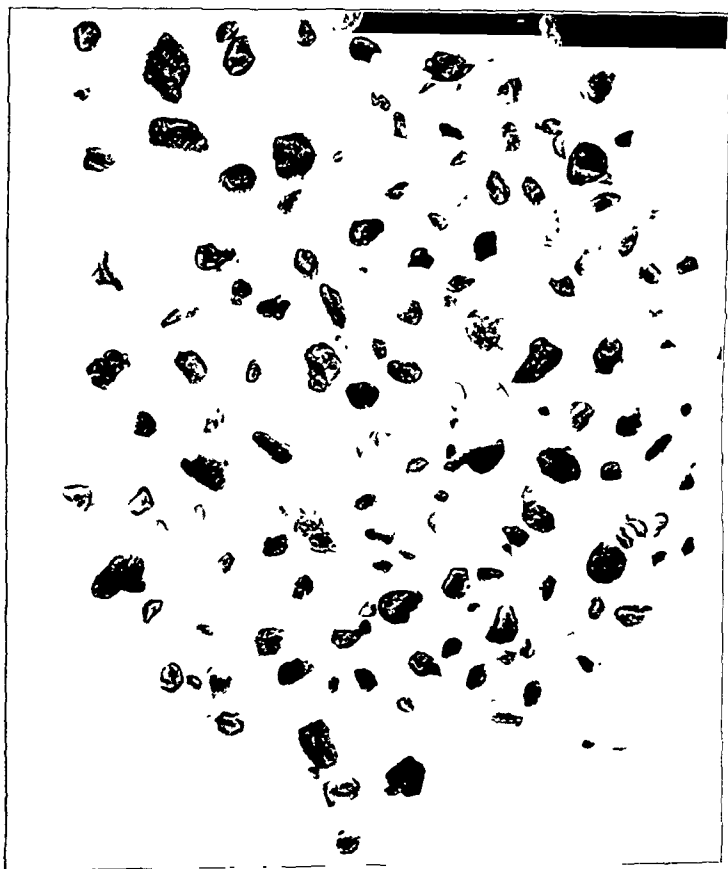


Fig. 17.

occurred inside the follicle, that is, internally and not toward the outside or externally. This will be more clearly shown when the follicles of the exophthalmic goiter are discussed. No junction or branching of any follicles occurred. They were entirely discontinuous and separate individual units. No evidence of any tubes or tubular formation could be observed. Small follicles would be grouped about the larger ones, but they always were dissected away with excellent cleavage and com-

plete separation, there being no continuity between the small and the large follicles. The roundness of the follicles and their rather symmetrical appearance gave the impression that they were completely filled with colloid, whether small or large, excepting the small ones in which there was scarcely a lumen, and that there was plenty of room in the gland for each follicle to become normally distended without

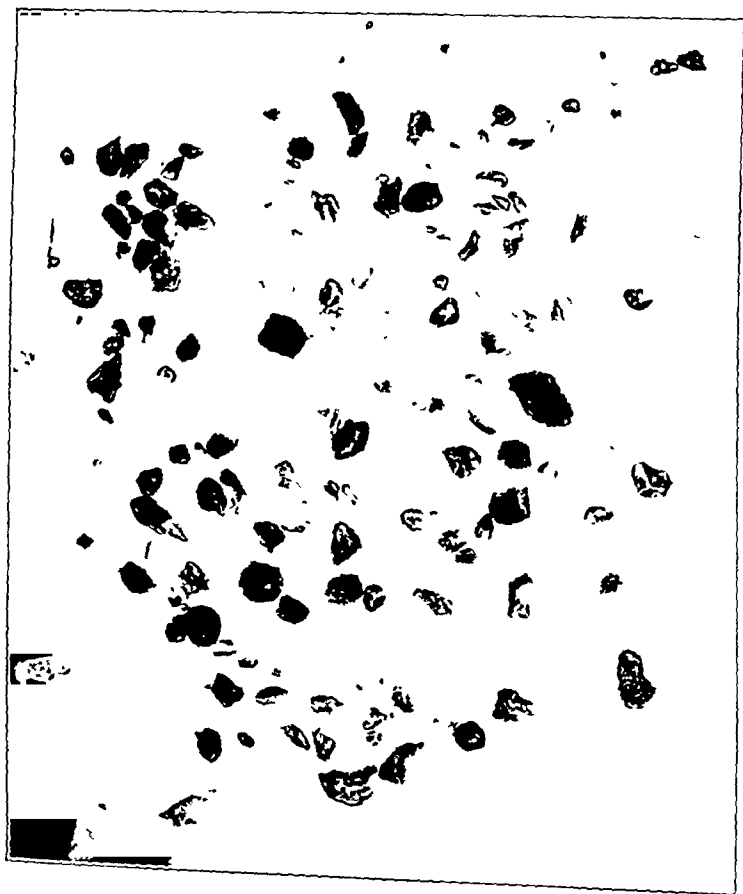


Fig. 18.

causing changes in the shape of each other by pressure. The follicles, though varying in shape and size, were all complete, distinct and fully differentiated histologic units. If the presence of colloid is an indication of function, then the larger follicles were carrying on the major part while the smaller ones were being held in reserve. It is highly improbable that a gland functions throughout its entirety at the same time. No evidence of any undifferentiated epithelial cell rests was made out from the maceration and dissection of the gland.

As has been said, the fibrous tissue capsule of the thyroid gland with the blood vessels and connective tissue septums were dissected away with great ease after fixation in Siehler-Heuser² solution and macerated in 5 per cent hydrochloric acid for one hour at 60 C. However, the follicles which collectively formed the parenchymatous tissue were bound together in close union by an interfollicular connective tissue which carried in its framework arterioles, capillaries, venules, lymphatics and nerves. This interfollicular connective tissue was much more difficult to dissect off from the individual follicles. There was no cleavage such as occurred in the removal of the main septums which divided the gland into many regions. The follicles could be dissected



Fig. 19—Isolated follicles from the exophthalmic gland from which the wax model in figure 32 was made. Note the smooth external contour and irregular internal surface. The clear area represents colloid into which finger-like prolongations of internal epithelial lining are protruding; $\times 86$.

away from a portion of a main region of the gland, but such sharp dissection with some force always endangered the follicles. Figure 7 represents a few follicles dissected in this manner in which the tags of connective tissue are still clinging to the follicles in spite of many attempts to clean them. So tenacious was this interfollicular connective tissue that a much stronger maceration was required and 50 per cent instead of 5 per cent hydrochloric acid was employed for one hour at 60 C. The more gentle blunt dissection then sufficed not only delicately to separate the follicles from each other, but also even to dissect

the capillary bed with the follicle. Figures 14 and 15 show the anterior and posterior views of the same follicle about which the injected capillary bed may be seen. On the one side is seen the vessel of ingress, and on the opposite side there is a similar appearing vessel. The anastomosing capillary bed invests the follicle completely. The apparent marginal gaping seen in figure 14 is due to the reflection of the light. Although not shown in this figure, the capillaries extend all around the edge of the specimen. The vascular bed about the follicle of the normal thyroid gland is thus shown to be very rich.

The Hyperthyroid Gland.—As previously mentioned, dissection of the tissue from the glands of patients suffering with hyperthyroidism or exophthalmic goiter was made simultaneously with that of the normal thyroid gland. The same technic was employed. Figures 16,



Fig. 20.—Saucer-shaped exophthalmic follicles dissected from the same gland as those in figure 19. The clear area represents colloid. Note the smooth external contour and irregular internal surface. The finger-like epithelial processes protrude into the lumen of the follicle; $\times 86$.

17 and 18 represent three different groups of follicles. In figures 16 and 17, the groups are from the same gland from which the wax model was made, while, in figure 18, they are from another gland. As happens in the normal gland there is great variation in shape and size of the follicles, but the follicles are on an average much larger in the gland from the case of exophthalmic goiter. The proportion of small to large follicles is definitely less in the exophthalmic gland than in the normal one. There are some follicles that are below the average normal size, but these are comparatively few. The groups of dissected exophthalmic follicles shown here are magnified 40 times and when compared with figure 11, which shows the normal group at the same magnification, it is readily noted that the average size of those of the

normal gland are definitely smaller. The more sharp definition of the exophthalmic follicles in the figures 16, 17 and 18 is interesting because the density or thickness of the epithelial walls of the follicle is directly responsible for the definition on the photographic plate. The epithelial walls of the exophthalmic follicles are all more dense and thick than the normal by virtue of the fact that the epithelial cells are columnar or cuboidal and in most follicles the epithelium is infolded into the lumen of the follicles. The increase in opacity is readily appreciated by comparing figure 11 with 16, 17 and 18. The size of the follicles varied as compared with the normal from 0.21 to 5 mm., showing that the variation in size of the exophthalmic follicles is much greater than that of the normal, as is also the average size. If these larger follicles of the exophthalmic gland were distended with colloid, as are the normal follicles, to the limit of their epithelial lining they would be even larger in size. The present increase of the size of these follicles seems to be chiefly one of an increase in the amount of epithelium since there is little colloid present. The total epithelial surface as well as the amount of epithelium present seems to be definitely increased. The colloid, of course, is diminished. The increase in the size of each individual follicle due to an increase in the epithelium results, in exophthalmic goiter, in an increase in the size of the gland due to an actual growth of the epithelium or parenchyma. The second departure from the normal noted in the exophthalmic follicles was in the shape. Here again, as in the normal gland, the shape of each follicle differed in some slight degree. No two were alike. The various shapes and forms encountered will be appreciated by a reference to figures 16, 17 and 18. In these all variations may be seen, from a long straight cylindric tube to a perfect sphere, and again from a cube to a hexagonal, octagonal, globoid, hatchet-shaped or pear-shaped unit. Near the center of figure 17 will be seen a delicate, straight, almost y-shaped, tubelike follicle and to the left of the figure a follicle the shape of the figure six. These and the straight cylinder were the only types of tubular follicles encountered in this study. There is a definite difference, however, in the shape of the exophthalmic follicles when compared with the normal. This difference is shown only poorly by the photographs, and really to study it one should move around the follicles under the binocular microscope. In figures 16, 17 and 18 the broad side of the follicles has been photographed, as narrow ones could not be made to balance on an edge. For this reason the thickness of these exophthalmic follicles is not brought out in the photographs. The follicles did not seem to have room for proper expansion in the exophthalmic gland as they had in the normal gland and were more flattened against each other, their long axes being parallel to the surface or long axis of the plate, bar or arm of parenchyma of which they formed a part. In this

sense there was a stratified arrangement of the follicles of the thyroid but the stratification is different for each distinct region. After dissection it was observed that these follicles were not completely distended with colloid but appeared to be only partly filled with a less viscid material which allowed their walls to bulge less than those of the normal follicles. The follicles from the surface of the gland were disposed to be more flat and saucer-shaped, while the ones from the inner zones of the gland were more apt to be elongated or even more spherical or spheroidal. The shape of the follicle is therefore dependent to a great extent on the region or zone of the gland from which it comes. The tendency toward flattening and also elongation in the exophthalmic follicles constitutes the chief difference between them and



Fig. 21.—Camera lucida drawing of isolated exophthalmic follicles, showing smooth external contour with very irregular internal surface. The thin epithelial roof or dome of this follicle is shown by the high lights, while the watery-like colloid inside the follicle is represented by the dark areas. Finger-like epithelial budding into lumen of epithelial lining is readily seen; $\times 40$.

the normal. It is to be noted that except for the minor irregularities in contour the external surfaces of the follicles of the exophthalmic gland are relatively smooth and as observed in the normal follicles there are no pseudopodial outpouchings of the epithelial sac, no budding off of new follicles, no constriction or cleavage of the primary into secondary follicles. Grouped about the larger exophthalmic follicles are usually to be seen small satellite follicles which, if a section was made across them, might appear to be the result of outpouching of the follicular epithelial sac. This is only an illusion, however, for these small, peripherally placed follicles are in no way connected with the larger more central follicle. The follicles are definitely increased

in size but are fully differentiated and developed individual and independent units. There was no continuity observed between them.

Figure 19 is a photograph of a follicle from the gland of a patient with exophthalmic goiter. By means of a finely ground pair of scissors the top or dome of this follicle was cut away so that one might look down inside. It is to be noted that the external form is almost perfectly smooth, whereas the internal surface is irregular as a result of the infolding of the epithelium. The finger-like epithelial projections

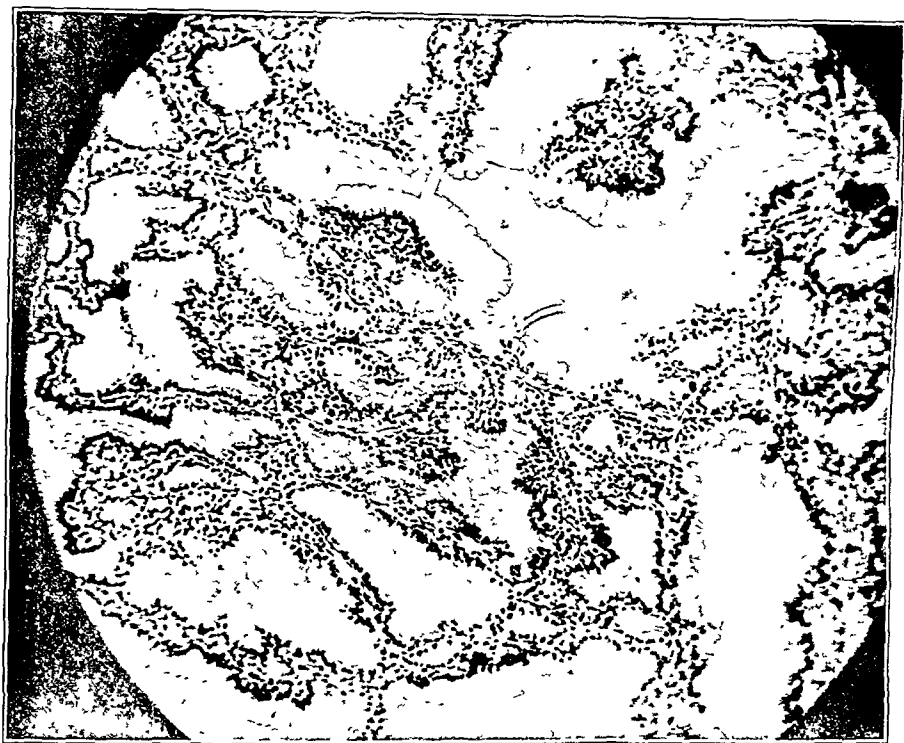


Fig. 22—Microscopic section of the exophthalmic gland from which dissection and wax models in this study were made. Section shows papillomatous infolding into the follicles in one plane while the dissected isolated follicle shown in figure 21 represents the internal and external form of the follicle in all dimensions and is more of a stereoscopic view of the papillomatous infolding; $\times 40$.

may be seen extending from the bottom epithelial rim toward the top where a very much thickened and irregular wall of epithelium exists. The right end of the follicle also shows a much increased epithelial covering. The clear area into which the papillomatous infoldings occur is the water-like colloid, the viscosity of which has been much decreased from that of the normal. This follicle is spheroidal. Figure

20 shows two saucer-shaped exophthalmic follicles from which the dome has also been removed. One looks down on them with the watery colloid covering the more opaque epithelial walls. Protruding up from the bottom may be seen several finger-like projections of the infolded epithelium. The external contours of these follicles are observed to be regular; the internal surface is very irregular. Figure 21 is a camera lucida drawing which accurately portrays the appearance of a single exophthalmic follicle. The relatively smooth external contour is to be noted in comparison to the very irregular internal surface. The thin

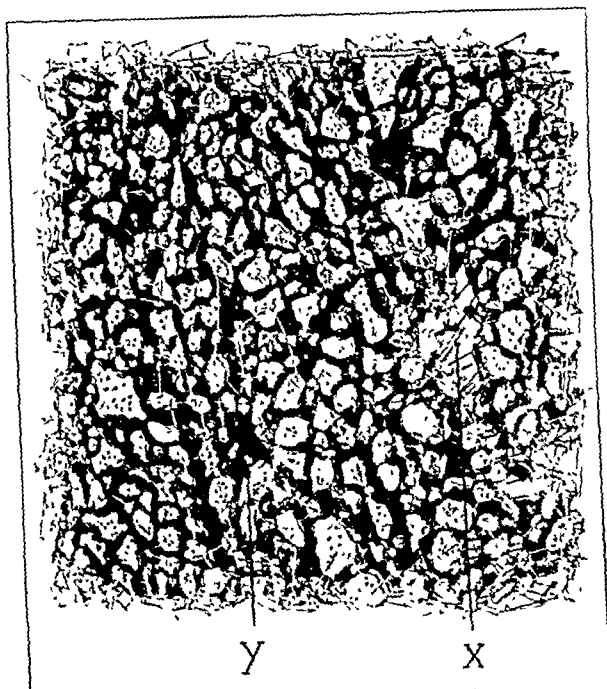


Fig. 23.—Top view of the half completed wax reconstruction of the normal thyroid. In the upper portion of the photograph can be seen the space corresponding to the fibrous connective tissue septums labeled *X*, and just below the middle on the right hand side is the course of another fibrous band labeled *Y*. These correspond to the similar tracts shown in figure 6. Reduced to $\times 21$ from $\times 75$.

epithelial roof or dome of this follicle is shown by the high lights and the dark area within represents the thin watery-like colloid into which the numerous buds or pseudopodial processes of epithelium have protruded. A section through the tissue of the same gland from which they were dissected is shown in figure 22 and the wax model to be described later was also made from the same gland. A comparison is in this way offered between a stained section of the follicle in exophthalmic goiter portraying the papillomatous infoldings in one plane and the dissected follicle showing the external and internal forms in

all dimensions. The study of the follicles by this latter method is obviously more accurate, affords a much better conception of the size and shape, the external and internal form with its blood supply than any other method heretofore employed.

RECONSTRUCTIONS IN WAX OF THE NORMAL THYROID AND
THE GLAND IN EXOPHTHALMIC GOITER

In a review of the reports of previous investigators, it is interesting to note the influence of the technic employed in examination of the thyroid gland on their opinions and conclusions. In the early studies

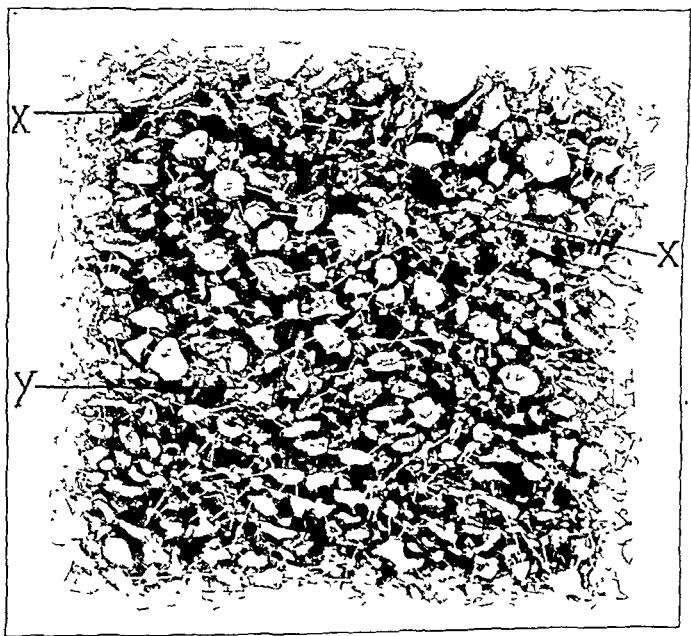


Fig. 24.—Top view of fully completed model before the removal of wires subtending the various follicles; $\times 21$.

erroneous conclusions were arrived at because only an examination of the individual sections was made. This stage was followed by the use of graphic reconstruction and then the more accurate wax plate models were constructed. In this study wax plate reconstruction was employed when the problem was begun three years ago, but it was soon recognized that while certain points of interest could best be shown by this method, there were others which could not be determined. The limitations of this technic will be pointed out in the following description of the models and also later in this paper.

The technic employed in the formation of the models has been discussed in detail and need not be repeated here. The wax models

were made in order to determine, if possible, the presence of a true lobulation of the gland as a whole; the manner in which the gland as a whole was subdivided; the ramifications of the fibrous tissue septums; the size, shape and spatial relation of the follicles; whether or not the follicles were connected or were discontinuous; the presence of interacinar fetal cell rests, and the distribution of the capillary circulation of the follicle. In spite of the fact that both the model of the normal thyroid and that of the exophthalmic gland were the largest which have ever been reconstructed, it was impossible by this technic to determine all of these points, and particularly that of the structure of the gland as a whole and the manner into which it is subdivided. The microscopic areas of the sections to be reconstructed were selected from two different points of view. In the normal gland the right angle edges of the section, and therefore their photographic plates, were used

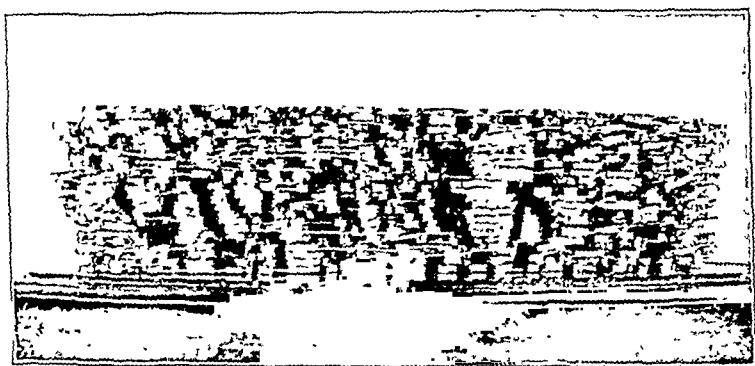


Fig. 25.—Profile view of the untouched model of the normal thyroid gland before the removal of wires. The great preponderance of small follicles may be seen in figure 25 as well as in figures 23 and 24. Largest follicle in entire model is shown in this photograph just to the right of the midline; $\times 21$.

as the guiding points for the reconstruction of a large corner area of the microscopic section. This area was marked off by the lines of orientation, and all epithelial structures as well as fibrous tissue septums which occurred in this area were carefully traced on the wax plates. In this way any tendency to lobulation of the parenchyma could be disclosed. Further, all epithelial structures in this large area were reproduced in wax in their natural spatial relation to each other so that the presence of any interacinar epithelial cell rests would be evident. This complete reproduction in wax of a large area was felt to be more convincing of the true detailed structure of the parenchyma and its constituent follicles with their relation to one another, than the reconstruction of just a few individual follicles as had been done in the past.

In the gland of the exophthalmic goiter, however, the microscopic field from which the model was to be made was selected in a different manner from that utilized in the case of the normal gland. In this instance the selection was made with special regard to a microscopic area in the middle of a section, midway in the series, an area which was apparently completely circumscribed by connective tissue septums and which was also apparently a separated and isolated lobule of the parenchyma of the thyroid. The orientation lines were, of course, drawn as for the normal thyroid, but the fibrous connective tissue septums which apparently completely surrounded the area of parenchyma served as the marginal guides of the tracings on the wax plates, and therefore, the boundaries of the model of the exophthalmic thyroid tissue were formed by the connective tissue septums. The external form of the model portrays the course of these septums within the gland. Only the follicles contained within the boundaries of this fibrous connective tissue were reproduced in this model of the thyroid in exophthalmic goiter. In this way the connection or junction of the parenchyma enclosed within the fibrous septums with the parenchyma of another portion or region of the gland would be evident. Therefore, any separation, fenestration or attenuation of the fibrous septums would be manifested in the wax model by the tendency of the follicular parenchyma to break or protrude through the connective tissue envelope. This, as will be shown later, occurs in the model of the exophthalmic goiter gland. Thus the models differ in size and shape because the margins of the normal model were formed first by the right-angled edges of the section which bound the corner area of the microscopic field selected for reconstruction; and secondly, by the opposite edges of the wax plate cut at right angles, and on which the tracings were made. In this way an almost perfect square model was obtained which is a reproduction of all the structures, epithelial and connective tissue, that occur in a specific blocked-out microscopic area of the section, without any particular reference to the fibrous tissue septums, whereas the model of the thyroid from a case of exophthalmic goiter is a reconstruction of the parenchyma with specific reference to the fibrous septums of a certain microscopic field, and the external shape of the model depends on the course and ramification of these septums. It is, therefore, not a square model, but has more of a tendency to an asymmetrical tubular form. The magnification is the same in both models, i. e., 75 times.

Model of the Normal Gland.—The wax model of the normal thyroid will be described first. For the sake of clearness it may again be said that the model was made by tracing each microscopic section on a wax plate, from which tracings the models of the follicle were cut out and wired together as shown in figure 6. These positive reproductions were then piled on one another according to the lines of

orientation. Thus positive wax models were made of each and every one of the stained serial sections. The positive models were piled on one another according to their lines of orientation to avoid any distortion of the model. A view of the top of the wax reconstruction when only half completed is shown in figure 23, and in figure 24 the same view of the fully completed model. Figure 25 shows a profile view of the finished model of the normal thyroid before many of the wires were removed and also before the wax casts of the follicles were smoothed off with an electrically heated needle and fine spatula.

In figure 6, although this is a wax reproduction of one section only, the preponderance of small follicles to larger ones is already evident and their average in diameter, shape and spatial relation could almost be predicted from this section. The course of a fibrous connective

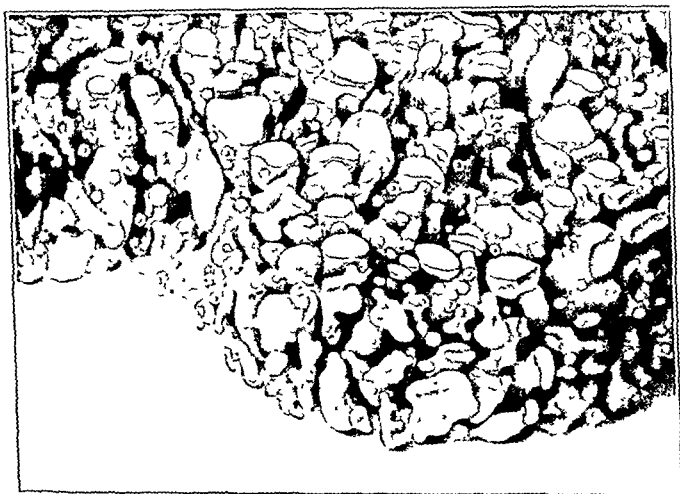


Fig 26—Drawing to scale of the wax model of the normal human thyroid. The model represents the internal shape of the follicles. The subtending wires are not included in the drawing. In the lower right corner may be seen one of the square sides of the model identified by the vertical or sagittal flattening of the incomplected follicles. Also the top of the model shows the incomplected follicles. The serpentine front is shown which represents an undamaged surface of the model and one including only completed follicles. This front was obtained by dividing the model along the course of the fibrous septums shown in figures 6, 23 and 24. Note the irregularity of the internal shape of the follicles, apparent budding, constriction and fission of the follicles. Also note the predominance of small follicles. It is at once evident that if sections were cut through this model at different levels some of the follicles would be sectioned at maximum and some minimum diameters. It is probable that sections through some of the smaller follicles or the dome of an underlying follicle might be misinterpreted as interfollicular or interacinar cell rests: $\times 45$

tissue septum can be seen in skeleton outline at the point *X* and, as will be shown, can be traced through the entire model. In looking at the wax reproduction of one section it is, of course, impossible to tell the cross-section of a very small follicle from a tangential section through the dome of an underlying although larger one. In figure 23, the wax model is only half completed. The course of the fibrous septum referred to in figure 6 can be traced in this model in the upper portion of the photograph. It is also labeled *X*. Just below the center there is shown the course of another fibrous band, labeled *Y*. The same division of the parenchyma by connective tissue can again be traced in figure 25, a photograph of the model after completion. The long septum *X* to the right side of the photograph and the shorter one to the left show up more clearly in figure 24 than in figure 23 because the former was photographed on a white porcelain plate, the latter on a plain glass plate.

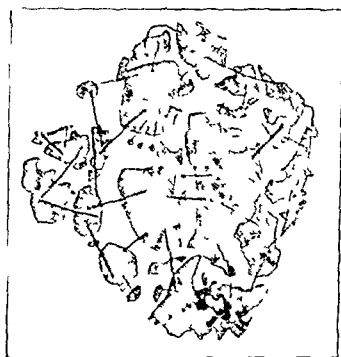


Fig. 27.—Wax model of a single section of exophthalmic goiter. Comparison with figure 6 from the normal gland demonstrates the great difference in size and diameter as well as shape of the follicles in exophthalmic goiter as compared with normal thyroid gland; $\times 30$

Figures 23 and 24 furnish an idea of the model in cross-section showing again the great preponderance of small follicles in comparison to the larger ones and their complete discontinuity in this horizontal plane. The small holes in the surface of the follicles in figure 23 are due to punctures with an electric needle made while fusing each successive layer so that some of the connecting wires might be removed. In figure 25, a profile view of the model, the preponderance of the many small follicles is again shown. The supporting wire of each individual plate remains. In figure 25 the largest follicle of the entire model is seen. It may be traced through all but a few sections of the block and is greater not only in length but also in width than any of the other follicles. The discontinuity of the follicles is again demonstrated in the vertical plane. Figure 26 is a drawing to scale of the

completed model of the normal thyroid gland. All but a few wires were removed with a pair of electrically heated forceps and the few remaining were eliminated from the drawing by the artist, Mr. James F. Didusch. It will be noted that the drawing is made at an angle which shows the top of the model and also the now serpentine margin in front with just a small portion of one of the square sides of the model in the right corner of the drawing. The tip end of this straight side can be identified by the vertical or sagittal flattening of the incomple-

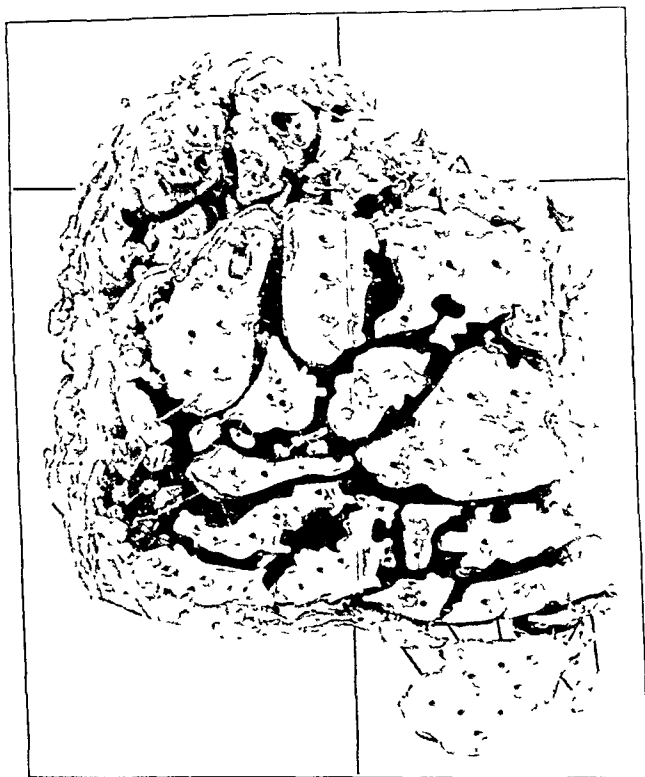


Fig. 28.—Top view of a half completed model of exophthalmic goiter. Note the irregularity in shape of the individual follicles; $\times 42$.

follicles along the edge of the model. The drawing was made in preference to a photograph because three sides or surfaces could be portrayed by it. In order to present an undamaged surface of the normal gland and also a surface in which no incompletable follicles would occur, as shown in the straight cut surface in the right corner of the drawing, the model was divided along the course of the fibrous septums *N* shown in figures 6, 23 and 24. This division resulted in the formation of the serpentine front to the model shown in figure 26 composed of only completed follicles. It will also be noted that the wax

casts of the internal shape and form of the follicles shown in figure 25 have been smoothed off in figure 26. This was done partly because of the better and more clear definition of the follicles in the model after smoothing and also because the stair-step-like overhanging edge of the tracing of the follicle in each section is in reality an inaccuracy and should be removed. This fusing and smoothing out of the individual wax models of the follicles was accomplished by means of electrically heated needles and spatulas. In order that no errors should occur, constant reference was made to the stained sections and photographic plates. The great number of small follicles in proportion to the larger ones is at once evident, and this fact is made more striking when the illustration of the model of the normal thyroid is compared with that of the gland in exophthalmic goiter. It is to be recalled that the wax models of the follicles represent the internal form or shape of the follicle because the inner margin of the epithelial sac composing the follicle was traced on the wax. In this cast the internal shape of the follicle may be compared with the external shape demonstrated by the dissection of the entire unit as shown in figure 11. The internal shape of the follicle is more irregular and less spheroidal than the external form which is, of course, due to the infolding of the epithelial wall into the lumen of the follicle. The smaller follicles seem to be much more regular in form, being spheroidal. There are occasional casts of a distinct tubular shape and some that branch slightly, as can be seen in figure 26. There are also follicles that seem to give off buds and others that are constricted, but again it is to be recalled that these casts represent only the internal form of the follicle and not the external. Almost all varieties of shape are to be seen in the model, but when compared with the dissected specimens the much greater tendency to tubular form, branching, budding and constriction is evident in the model. The greatest variability in size is shown, from follicles 1.5 mm. or even less in diameter up to 35 mm. There is complete discontinuity of the follicles. No coiled tubules were encountered in the normal gland. No sign of junction between the follicles could be detected. The spaces between the follicles appear greater in the model than they actually are in the gland because only the inner margin of the epithelial wall was traced, and consequently the thickness of the follicle wall is lost in the model. The remaining space is normally filled with blood vessels, connective tissue, lymphatics and nerves. No evidence whatsoever was educed in regard to so-called interacinar fetal cell rests. There are no epithelial cell rests of any type in the normal thyroid gland of the adult. The only epithelium encountered in the thyroid was a fully differentiated variety which formed a definite part of the parenchyma; even in the smallest follicles

in which a lumen is scarcely visible the epithelium is arranged in the usual manner of thyroid epithelium and appears to be fully differentiated. It is obvious from figure 26 that if serial sections were cut through the model some follicles would be cut through at their maximum diameter while others would be cut tangentially only across their dome without even disclosing the lumen of the underlying follicle. This, of course, would give the impression of a group of interacinar cells apparently disconnected from the remaining parenchyma of the thyroid but would only be an illusion, for if the continuation of the series is followed it will be found that what appeared to be an isolated group of interacinar epithelial cells was merely the dome of an underlying follicle. In some instances, when the follicle is almost a true sphere in which the diameter is only 20 microns or even less, a series of sections 10 microns in thickness may be necessary to prove the follicular arrangement of the lining epithelial cells. In this study the serial sections of 20 microns in thickness were used to determine this point, and also for the reconstructions in wax; in addition, a series of sections cut 10 microns in thickness was studied for the presence of interacinar cells not a part of the parenchyma. The casts of the follicles of each section and the model as well were carefully checked with the serial sections in the series cut 20 microns in thickness to avoid the error of overlooking possible epithelial rests and clusters of interacinar cells. A graphic microscopic study was made of the other series of sections cut 10 microns in thickness, but not the slightest evidence was educed from either series even to suggest the presence of undifferentiated or differentiated epithelium between the follicles and not connected with, or a portion of, the parenchyma of the thyroid.

Even though the model shown in figures 23 to 26, inclusive, is the largest wax reconstruction ever made of the normal thyroid gland, it is at once evident that the structure of the thyroid as a whole and the manner in which it is subdivided into various regions cannot be learned from such a small area of the gland. Investigators in the past, some working only from single sections, others with very small models consisting of only a few follicles at an unnecessarily high magnification, have unhesitatingly described the thyroid as a lobulated gland. The structure of the gland as a whole and the form of its many subdivisions could not be learned from this model of the normal thyroid gland, simply because the block of tissue from which the serial sections were cut was far too small for this purpose. It is interesting to note that although this model is a complete reproduction of a much larger microscopic field than heretofore has been reconstructed in wax, and at the same time is the only model in which all the follicles of a given area have been included, yet it is impossible to discern any tendency

toward lobulation of the gland. Previous reports, although based on much smaller models of only a few of the larger follicles, overlooking the smaller ones, however, have concluded that the gland is definitely lobulated.

The Thyroid in Exophthalmic Goiter—In the wax plate reconstruction of a portion of the thyroid gland from a case of exophthalmic goiter the same technic was followed as described for the normal gland.



Fig. 29—Top view of completed model of exophthalmic thyroid, $\times 40$ Compare with figure 28

The only difference lay in the method of the selection of the microscopic field for reproduction in wax. An area was chosen which apparently consisted of a group of follicles completely surrounded and isolated by fibrous connective tissue. This area was similar to those which in the majority of textbooks on histology are referred to as a "lobule." Furthermore, this microscopic field was located in a section toward the middle of the series so that one could build up or down in the series and follow this localized area through to its conclusion. Figure 27 is a photograph of the microscopic field reproduced on a bromide plate

transposed into wax casts of the follicles enclosed in the fibrous septums. The latter were not included in the tracing onto the wax, but all the follicles enclosed were included so that the external form of the model corresponds to the course of the fibrous envelope in the substance of the gland. In this way any tendency on the part of the fascia to become attenuated and fade out or to disappear into the surrounding parenchyma is evident in the sections and manifested in the model by the widening or spreading out of the original follicular grouping into a larger or rather branched group. The original small group of follicles circumscribed by the fibrous septums would become connected with contiguous parenchymatous areas; the latter in turn incompletely enclosed between other fibrous connective tissue bands would form con-

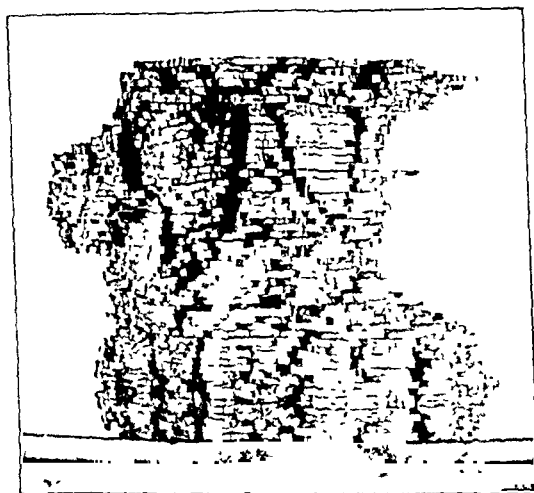


Fig. 30.—Profile view of untouched wax model of the thyroid from the case of exophthalmic goiter. The external contour of this model demonstrates the tendency of the parenchyma of the gland to branch into other regions by attenuation and spreading out of connective tissue septums. Wire struts support these offshoots or connecting bars of parenchyma; $\times 44$.

nections with still further regions of parenchyma and so on ad infinitum as shown in the dissected specimen. Figure 27 illustrates the variations in shape and size encountered in the wax reproduction of the internal form of the follicles of the average section of the thyroid in exophthalmic goiter. This section was taken from the middle of the series and portrays the small group of follicles enclosed in the connective tissue envelope. When compared with figure 6, a similar photograph of the normal gland, it is at once evident that the average diameter of the follicles is much increased in the exophthalmic gland. The irregularities in contour due to infolding of the epithelium are also evident. Figure 28 is a top photograph of the model a little more than half completed.

The orientation lines on the glass base and scratched in the wax of the model may be seen as well as the fusing holes caused by piercing the wax models with the electrically heated needles. In the upper portion of the photograph may be seen the apexes of some follicles which have been completed at a lower level than the top plate of the model. These suggested a plateau, quite a distance below the top section of the model. The latter wax plate represents a section of the series a little more than half way through the middle of the model, and the outside edge or margin of this middle section corresponds with the position of the fibrous septums enclosing the follicles at that level in the gland and on the model. This also applies for each section. The shape of the model, therefore, exemplifies as a whole the form of the region of parenchyma enclosed by the septums. About the middle of the model

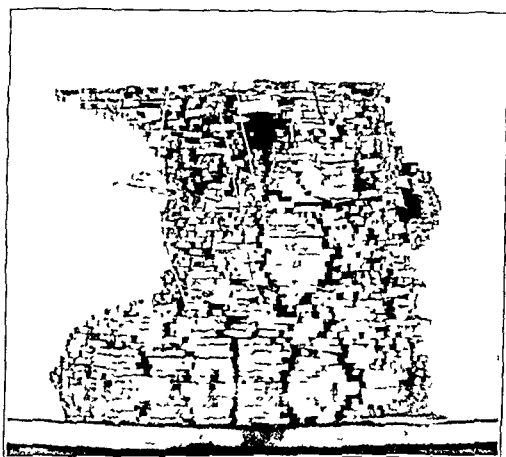


Fig. 31.—Another view of the profile view of the concluded but untouched model from the case of exophthalmic goiter. Note the spaces between the follicles and the stair-step appearance due to the piling of the plates; $\times 44$.

the transverse area of follicles completely enclosed by the connective tissue bands is less in diameter than at any other level in the series. As will be noted in figures 28 to 31 inclusive, there is an irregular enlargement of the model at both the top and bottom. This is due to an increase in the number of follicles within the circumscribed area of connective tissue, or in other words to an enlargement of the space enclosed by these septums due to their separation or spreading apart. In figures 28 and 31 the lower plateau formation, in the upper portion of the photograph, is due to the increase in the size of the original group of follicles as the septums gradually fade out into the small strands of interfollicular connective tissue. At the top level in the lower portion of the photograph can be seen the tendency of one corner of the

model to spread out from the original shape. A top view of the finished model shown in figure 29 demonstrates this branching out, budding or spreading of the parenchyma very well. The profile views of the untouched model emphasize the tendency of the so-called "lobules" or original group of follicles to spread out and become joined with other regions as shown in figures 30 and 31. Wire struts were necessary to support these off-shoots of follicles. The narrowest region of the model is toward the middle, and it was here, in the stained sections, that the encircling fibrous connective tissue septums stood out most strikingly and completely surrounded the smallest group of follicles. Just as illustrated by the model, as one progresses from the

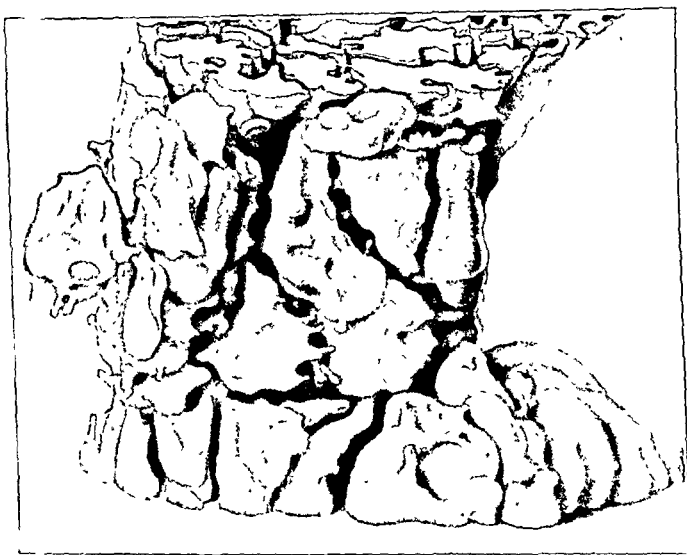


Fig. 32.—Drawing to scale of the finished model of the thyroid in exophthalmic goiter. Compare with figure 26, which is the completed model of the normal thyroid gland. The irregularity in shape and the much larger size of the individual follicles of exophthalmic goiter as compared with the normal are at once evident and the preponderance of small follicles in the normal thyroid is striking when compared with the almost total absence in the exophthalmic gland. Indentations of the wax model of the case of exophthalmic goiter are due to papillomatous infolding of the epithelium; $\times 75$.

middle of the series toward either end, in looking at the stained sections, the fibrous septums become thinner, less pronounced and at the same time spread further apart. Concomitantly, they enclosed a greater number of follicles until there is such an attenuation and fading of the septums that they are reduced at certain points to small strands indistinguishable from the interfollicular connective tissue. It is at these points that there is a junction of the primary trunk of parenchyma

with other portions of the gland. The connecting bars are shown in the model as the projections of groups of follicles mentioned. From this it is evident that the apparent lobule of parenchyma of the thyroid completely surrounded and isolated by the bands or septums of connective tissue was an illusion, for if the model, and especially the stained serial sections are examined, it is at once evident that the connective tissue septums traverse the parenchyma of the gland in a very irregular manner and do not separate the thyroid into lobules. In the model of the thyroid tissue from a case of exophthalmic goiter, as in the case of the normal thyroid, there was no evidence of lobulation. Figure 32 is a drawing to scale of the finished model of the thyroid in exophthalmic goiter. The drawing was made at an angle that would permit a portion of the top of the model to be drawn, so that a transverse and longitudinal view of some follicles was obtained. The follicles have been smoothed off as in the model of the normal gland. It is again to be recalled that the wax casts shown correspond to the internal form of the follicle and the hollow indentations are due to the papillomatous infoldings of the epithelial lining into the lumen of the follicle. The follicles are on the average larger than those of the normal gland and their internal surface is relatively much more irregular. This irregularity is well shown in both the lateral and the top view. There are a few small follicles, but they are most conspicuous by their great diminution as compared with those of the normal thyroid (figs. 6 and 26). The magnification of both the normal and the exophthalmic models was 75 times. The internal shape of the follicles as seen in figure 32 varies a great deal but all are more or less spherical or spheroidal. Some are more flat and narrow, others rather shorter and of a greater diameter. Apparently the follicles in the center of the group are less flattened than those immediately adjacent to the connective tissue bands. There was no evidence of any outpouchings or pseudopodial-like protrusions of the follicles. They were all separate and distinct units completely disconnected. No tubular forms or coiled tubules were encountered in this model. There were no interacinar fetal cell rests or islands of epithelial cells disconnected or disassociated with the parenchyma of the thyroid. This point was again carefully checked in the series of sections 20 microns in thickness from which the wax model was made and also in another series cut from the same gland at a thickness of 10 microns.

COMMENT

Lalouette,³ in 1750, first called attention to the minute structures of the thyroid gland by stating that the vesicles seemed to communicate

3. Lalouette, cited by Boechat: *Recherches anatomiques sur la glande thyroïde. Mémoires de mathématiques et de physique présentés à l'académie royale des sciences (savants étrangers)* 1:159, 1753.

with each other. Later, in 1836, Jones⁴ described the thyroid follicles in considerable detail as completely closed vesicles. Bardeleben,⁵ in 1841, also concluded that the adult thyroid follicles were completely isolated structures. In spite of these two contributions, the majority of observers, such as Cruveilhier,⁶ Virchow,⁷ Boechat,⁸ Zeiss,⁹ and Hitzig,¹⁰ followed Lalouette³ in describing the follicles as forming a system of branched and communicating cavities within the gland. These opinions were all based on relatively inexact methods including observations on microscopic sections which were not cut in series. Such observations made on isolated sections of the gland were misleading and allowed of a great latitude of opinion which varied with personal interpretation. Streiff,¹¹ in 1897, was the first to employ an exact method when he adopted the technic of Born or the wax plate reconstruction method for the study of the normal human thyroid. He concluded that both isolated vesicles and branching forms occur in the normal thyroid although these vesicles do not form a system of communicating cavities throughout it. He found that the follicles were ovoidal or spindle-shaped, but that branched forms due to budding or secondary fusion were also encountered. Streiff¹¹ modeled only a few individual follicles separately, and did not investigate their relation to each other or to the gland as a whole. He used the inner epithelial margin of the follicle in tracing the outline of the vesicle on the wax so that his conclusions as to the shape of the follicle are based entirely on the internal and not on the external form. In 1923, Williamson and Pearce¹² conjectured that the thyroid organ consists of two lateral lobes joined by an isthmus. They stated:

The lobes of the thyroid are composed of an aggregation of lobules lying in the meshes of the interstitial tissues of the organ. The parenchyma of the lobule

4. Jones, C. H., in Todd: *Cyclopaedia of Anatomy and Physiology*, vol. 4, pp. 1102-1118.

5. Bardeleben, S., cited by Zeiss: *Observationes microscopicae de glandularum ductu excretorio carentium structura deque earundem functionibus experimenta*, Diss. Inaug., Berlin, 1877.

6. Cruveilhier, J.: *Glande thyroïde*, in *Traite d'anatomie descriptive*, ed. 2, Paris, vol. 3.

7. Virchow, R.: *Die krankhaften Geschwülste*, vol. 3, part 1.

8. Boechat, P. A.: *Structure normale du corps thyroïde*, Thèse, Paris.

9. Zeiss, O.: *Mikroskopische Untersuchungen über den Bau der Schilddrüse*, Diss., Strassburg, 1877.

10. Hitzig, cited by Streiff: *Beiträge zur Histologie und Histogenese der Struma*, Diss., Zurich, 1897.

11. Streiff, J. J.: *Ueber die Form der Schilddrüsen Follikel des Menschen*, Arch. f. mikr. Anat., vol. 48, p. 579.

12. Williamson, G. S., and Pearce, I. H.: *The Structure of the Thyroid Organ in Man*, J. Path. & Bact. 26:459, 1923.

is divided up by loose strands of fibro-elastic tissue into a series of well defined functional areas or gland units. The fibro-elastic tissue forms a capsule which completely circumscribes each gland unit and carries the intralobular blood and lymph vessels. . . . The loose fibro-elastic tissue capsule of each gland unit is lined by a pavement endothelium. The serous cavity so formed is directly continuous with the intra-lobular lymphatic channels. . . . The epithelium of the gland unit appears in the sinusoidal space as long cylindrical columns. Generally these twist and turn in various planes to accommodate themselves to the circumscribed area of the sinusoid. . . . Concisely stated, therefore, the functional gland unit of the thyroid organ is essentially a lymphatic sinusoid in which float columns of epithelium enmeshed by a highly specialized plexus of blood capillaries.

Williamson and Pearce,¹² by reverting to the inexact methods of the early observers before the time of Streiff,¹¹ fell into the same pitfalls and traps by drawing conclusions from the examination of occasional and not of serial sections. They assumed a lobulation of the gland which does not exist, and there is no evidence of any coiled cylindric columns in a lymphatic sinusoid in either the dissected or the reconstructed specimens. However, despite their errors, they deserve a great deal of credit for stirring up new interest in the subject, and their work exercised what may be termed an enzymatic action. Wilson,¹³ in 1927, reported his observations on the thyroid follicle in man in the normal and pathologic conditions and successfully refuted the assertions of Williamson and Pearce.¹² He employed the reconstruction in wax previously originated by Streiff¹¹ in 1897. Wilson¹³ corroborated Streiff's¹¹ observations for the normal thyroid follicle, but went further and modeled a few individual follicles from a hyperplastic and also from a colloid gland. Streiff¹¹ had selected the follicles he modeled from entirely different regions of the microscopic section. Wilson's¹³ models contain a few more, from ten to twenty, follicles selected from a block of thyroid tissue from 0.3 to 0.6 mm. in dimensions. Although this number is slightly greater than was contained in Streiff's¹¹ reconstruction, it seemed to me preferable to include all the epithelial structures in a larger and more representative area of the gland by using a larger block of thyroid tissue. And further, it was decided to reconstruct all the follicles in that region in their exact relation to each other and not be satisfied to include so few as ten or twenty follicles from a given area. The study of only a certain number of follicles from an area, instead of all follicles or epithelial structures large and small occurring in that region, gives a less accurate impression of the variation in their size. Again, when the small follicles are eliminated in favor of the larger ones, one gets an entirely different impression of the composition of the parenchyma of that area. Wilson,¹³ as well as Streiff,¹¹ made the drawing

13. Wilson, G. E.: The Thyroid Follicle in Man: Its Normal and Pathological Configuration, *Anat. Rec.* **37**:31 (Nov.) 1927.

for the model from the inside of the follicle, the free margin of the cells being used as a guide line. The former said: "This method has been followed, because it separates the follicles sufficiently to permit their entire extent to be seen, yet preserves their actual shape." But this, of course, revealed only the internal form of the follicle, which Streiff,¹¹ and later Wilson,¹³ erroneously interpreted as the external shape. For this reason conclusions as to the budding, constriction, fusion or division of the follicles made first by Streiff¹¹ and later by Wilson¹³ are incorrect, because they are based on the internal instead of the external shape of the follicle. As shown in this study by a comparison of the wax models, the internal form of the follicles, and the dissected specimens, or external forms of the follicles, differ widely in shape. Relatively few, if any, irregularities in the external contour of the follicles were observed. There was no evidence of budding, fusion, constriction or division of the follicle when seen and examined in its entirety. When only the casts of the inside of the follicle were studied, as in the wax reconstructions, many pronounced irregularities were seen, but such internal irregularities have no significance as to the activity of the unit or vesicle in the formation of new follicles. The only significance which can be attributed to the irregular internal shape is an increased proliferation and growth of the epithelium into the lumen of the follicle.

The great preponderance of small follicles in the wax model of the normal gland as well as in the dissected specimens, in proportion to large ones, is suggestive, at least, that the thyroid tissue is completely differentiated in the adult, and after puberty the number of follicles is probably not increased by the growth of secondary vesicles from primary follicles. The small follicles would seem to form a reserve supply of parenchyma which, when called on to function, does so by an increase in size due to hypertrophy and hyperplasia of the epithelium. This is further borne out by the lack of evidence of any new follicle formation, such as budding and division, in the smooth external contour of the dissected follicles and also the pronounced decrease in the proportion of small to large follicles in the exophthalmic gland. Wilson,¹³ although having sectioned a small block not more than 0.3 and 0.6 mm. in thickness, said: "The dotted line in figure 4 represents the connective tissue septum enclosing the lobule," and went on further to discuss "the lobules." As shown by the reconstruction of a much larger (4 mm.) block, in this study, areas apparently completely surrounded by fibrous connective tissue septums, and thus forming a lobule, appear to exist only apparent for a few sections and are thereafter an illusion. In the reconstruction of the gland in exophthalmic goiter the fibrous septums were used as guide lines, and it was

demonstrated that the septums, in progressing through the gland, became separated, divided and attenuated and finally blended with the interfollicular fascia. In no instance in the wax reconstruction or the microdissections made was there the slightest suggestion of a lobulation of the gland. The group of follicles apparently surrounded by connective tissue always widened out and spread into other regions of parenchyma as a result of the irregular ramifications of the septums, so that the apparent circumscription of an area of parenchyma was always found to be an illusion. I am convinced, therefore, that the larger 4 mm. block of tissue cut serially in sections 20 microns in thickness reveals the error which may be made from conclusions based on evidence obtained from serial sections of too small a block cut 10 microns in thickness. A block of tissue of this size is not large enough to include a sufficient amount of gland to justify an opinion on the architecture of the thyroid as a whole.

It seems evident, then, that all of these investigations in the past have been concerned chiefly with the individual follicle and that in them the internal form of the vesicle has been considered the external form or true shape. As a result of this mistake conclusions as to the continued formation of new follicles in the adult, based on irregularities in the form or shape of the follicles reported in the past, are incorrect, because these irregularities occur only inside the follicle. The absence of these irregularities from the smooth, regular external form of the follicles, when dissected out in their entirety, would rather suggest that the probable growth of the gland occurring in the adult is due to the enlargement of follicles already formed rather than to the development of new or secondary ones.

Julius Casserius¹⁴ was the first to describe the thyroid as a simple organ consisting of two parts. Bartholomaeus Eustachius¹⁵ later described the organ as single, and gave to the structure joining the lateral lobes the name of isthmus. Since that time until the present there have been no reported studies on the structure of the entire gland and the character of the regions into which it is divided. As shown in this study, the lobes of the thyroid are irregularly broken up into regions or areas of tissue which are all joined together by connecting or annectent bars of parenchyma. In other words, the thyroid gland is divided, separated or honey-combed by an irregular system of communicating cavities which ramify all through it and until the gland is dissected these cavities are filled with tissue of mesenchymal origin and nerves.

14. Casserius, Julius: *De vocis auditusque organis historia anatomica*, Ferraria, 1600-1601.

15. Eustachius, Bartholomaeus: *Tabulae anatomicae*, Romae, 1714.

The parenchyma of the thyroid consists of large areas in the shape of bands, plates, bars, stalks and bulbs which are joined together by connecting arms, annectent bars or slender twiglike processes of thyroid tissue. These areas, in turn, are composed of individual discontinuous spheroidal or ovoidal follicles which are held together in a network of fibrous connective tissue. Blood, lymph vessels and nerves ramify in this network of interfollicular supporting tissue. There is not the slightest suggestion of a true lobulation of the thyroid gland; there is only a mass of thyroid tissue which has been irregularly broken up by a complex system of cavities later filled with mesenchymal tissue. An embryologic basis for this rather unusual manner in which the thyroid is subdivided has been shown by Norris¹⁶ in his study of the human embryo. After complete separation of the thyroid from the pharynx the gland grows rapidly and forms a bilobed platelike mass, thick and irregular, ventral to the trachea and in a plane parallel to the long axis of the body. At this stage, in 7 mm. embryos, the primordium is usually from about five to six cells thick in cross-section, and, according to Norris,¹⁶ there appear in this gland mass a number of completely closed cavities, at first tiny clefts, which suggest that the cells about them had pulled apart and they had apparently resulted from cracks or splitting of the tissue. These cavities increase in size and are brought more closely together. They vary markedly in shape, size and general position in the same and in different fetal thyroids. They have no visible content, but possess a distinct sharp outline. As growth continues these cavities become confluent, and finally as they open to the outside they are invaded by the adjacent vascular mesenchyme. The gland mass which was at first a solid body in the embryo is transformed into one that is hollow and the cavities of which are surrounded by epithelial plates. As a result of this process the gland comes to be made up of smooth epithelial platelike regions of parenchyma which unite freely with each other and ultimately come to form an extremely complex structure. Later, additional plates are formed by a process of budding and growth from plates created primarily in the initial breaking up of the gland mass. This transformation has occurred in the pre-follicular stage. The morphogenesis of the thyroid follicles of the chick has been reported (1929) by W. Bradway,¹⁷ who corroborated the observation on the human embryo made by Norris¹⁶ in stating:

By growth of cells and differentiation, the original impaired anlage becomes two solid bodies which, at the end of six days, contain nonfollicular spaces into which the mesoderm enters. At the end of eight days each glandular body has become a fenestrated labyrinth of parenchyma two cells thick.

16. Norris, Edgar H.: *Am. J. Anat.* 4:443, 1918.

17. Bradway, Winifred: Abstract no. 2216, Wistar Institute Bibliographic Service, no. 114, Feb. 28, 1929, to appear in *Anat. Rec.*

From this study it would seem that the irregular subdivision present in the human embryo persists into adult life. It was found that the greatest variations in shape and size occurred not only in the subdivision of the same gland but also in that of different ones.

It is interesting to note how, when once entrenched in the textbooks, a statement is handed on for a long time unchallenged. In 1883, Wolfler¹⁸ described rests of fetal cells between the follicles which he thought persisted into adult life and later gave rise to tumors or neoplasms of the thyroid gland. These have been referred to as inter-acinar, intervesicular as well as interfollicular cell rests. Wolfler examined only isolated sections, rather thick and poorly stained, for the technic of cutting sections in series was not known at that time. It is, therefore, quite comprehensible that Wolfler's methods were inexact and his conclusions inaccurate. In the present study after a most meticulous examination has been made of two series of sections, one cut 10 and the other 20 microns in thickness from both the normal thyroid and the gland taken from a case of exophthalmic goiter, not the slightest evidence of cell rests, either fetal or adult, between the follicles could be found. Only completely differentiated epithelium was encountered in the thyroid, and further, the only epithelium found was associated with some follicle presenting the normal appearance and arrangement of the adult thyroid parenchyma. The only possible explanation of a manner in which such a misinterpretation as Wolfler's could have occurred and also for the persistence of the same mistake as shown by many, even recent, articles is that a tangential section through the dome of an underlying follicle sometimes gives the impression of a group of disconnected epithelial cells. As a matter of fact, if the section is one of a series, it can be proved that the disconnection of the epithelium is only apparent and that the next section shows them associated in the formation of a follicle. It is believed, then, that this study justifies the conclusion that there are no such epithelial or fetal cell rests in the thyroid gland, whether it is normal or whether it comes from a case of exophthalmic goiter, and that the persistence of any type of fetal tissue in the adult thyroid does not occur.

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THE GALLBLADDER

ITS FUNCTIONS AND SOME OF THEIR DISTURBANCES IN THE LIGHT OF RECENT INVESTIGATIONS *

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The purpose and functions of the biliary vesicle are still debated problems (Mann,¹ Haberland,² Rost,³ Lütken's,⁴ Chiray and Pavel,⁵ Pfuhl,⁶ Westphal and Schöndube,⁷ Boyden,⁸ Blond,⁹ Babkin,¹⁰ Körte,¹¹ Moynihan,¹² Lyon,¹³ Whitaker,¹⁴ Rolleston and McNee¹⁵). The view most widely accepted regards the gallbladder as a reservoir the function of which is to supply concentrated bile whenever there is call for such in the intestine. This traditional concept, however, as may easily be gathered from the literature, does not provide the best explanation for such phenomena as the formation of biliary concretions and hydrops of the gallbladder, nor does it account for the occasional absence of clinical signs or symptoms in the presence of gallstones, and the not infrequent occurrence of typical signs and symptoms of cholelithiasis in the absence of concretions.

The appreciation of this fact, i. e., that the current notions of the function and dysfunctions of the biliary vesicle were difficult to harmonize with a number of well established clinical observations, was perhaps the principal reason that induced the German Surgical Society in 1923 to have a symposium on the gallbladder at their yearly congress in Berlin. John Berg, the Nestor of the Scandinavian surgeons, author¹⁶ of a new theory of the function of the gallbladder, was to deliver the opening address. This appeared in the transactions of the society,¹⁷ but was not presented because of the author's illness. Aschoff, who took his place, summarized the state of knowledge of the subject.¹⁸ His address is included in the volume of lectures which he delivered in this country in 1924.¹⁹ On listening to this address, one was struck by the emphasis that he laid on the resorptive powers of the gallbladder mucosa. His statements were based not so much on work in his own laboratory as on the experimental results of Rous and McMaster of the Rockefeller Institute.²⁰ The work of these authors marks the commencement of a new epoch leading to the present better understanding of some of the

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principles underlying the functions and dysfunctions of the biliary vesicle. When their experimental results were evaluated, it became clear at once that disturbance of the resorptive function of the gallbladder was the factor leading to stagnation of bile in the viscus, and not obstacles of a mechanical nature hindering free in and outflow—that is, the exchange of bile in the biliary vesicle—as was formerly advanced by Aschoff and Bacmeister.²¹ Thus, the concept of one of the generally accepted fundamental causes of the formation of gallstones—biliary stasis in the gallbladder—suffered a rather radical change.

Much impressed by the bright light thrown on the subject by this sudden discovery, I reconsidered the morphologic data and some of the experimental and clinical observations that I had collected from 1921 to 1923. This resulted in my becoming thoroughly convinced that the old conception of the function of the gallbladder was inadequate to explain its dysfunctions, and I began to question seriously whether the bile which once entered the gallbladder ever left it again through the cystic duct. Believing that, after three years' study of the biliary system, I had sufficient data to justify a new suggestion concerning the function of the gallbladder, I presented the idea in February, 1924, before the Society of German Physicians in Prague.²²

Sweet in Philadelphia delivered a Mütter-Lecture in December, 1923, entitled "The Gallbladder; Its Past, Present and Future."²³ In this lecture, which was published six months later, Sweet advanced much the same idea as mine, i. e., that the bile which once has entered the gallbladder does not under ordinary conditions leave it again through the cystic duct, but is resorbed by the mucous membrane of the biliary vesicle, and the constituents then returned by the way of the veins and lymphatics into the liver and the general circulation, respectively. While both of us agreed that the bile entered the gallbladder not to be stored there and in time expelled but to be resorbed in toto by the gallbladder mucosa, our interpretations as to the service rendered by the gallbladder through this function were somewhat different. According to Sweet's conception, the main function of the gallbladder was to play a part in the cholesterol metabolism. It is of interest to recall in this connection that Virchow²⁴ was the first, in 1846, to notice the presence of lipoidal substances in cells of the gallbladder mucosa. He regarded these cells later (1857) as being concerned in the intermediate metabolism of fats, considering a part of the fat of the bile to be resorbed by the gallbladder mucosa. Thus, Virchow concluded about seventy years ago that "the gallbladder is not a mere reservoir but has a further function, for through it fats find an intermediate passageway back into the circulation."

My conception was that the gallbladder performs at least two main functions: first, the return of important constituents of the bile into the circulation, and second, by the resorption of bile, the relief and

regulation of the pressure within the biliary system while the sphincter of the ductus choledochus is closed.

This was, then, the state of affairs about the beginning of 1924, when cholecystography was still in the hands of the discoverers and, indeed, in an early experimental stage. Cholecystography, the ingenious invention of Graham and Cole²⁵ for rendering the gallbladder content opaque to the roentgen rays, opened a new field for the study of the function of this organ and quickly became a most valuable addition to the list of indispensable methods of clinical diagnosis. It would lead, however, too far afield to review, and perhaps it would be too early to evaluate, the wealth of accomplishment since cholecystography became a routine clinical procedure.²⁶ Nevertheless, it may be said that in spite of the refined technic in producing shadows and estimating the amount of the content of the gallbladder,²⁷ most of the problems in regard to the function of this organ are still under active discussion. One investigator, Blond²⁸ of Vienna, recently emphasized the fact that interpretations of the results of cholecystography are easier and the manifestations less contradictory if it is assumed that the bile enters the gallbladder not to be stored there and in time expelled, but to be resorbed in toto by the gallbladder mucosa. With this I agree. The fact that bile may and does leave the gallbladder occasionally in small quantities does not invalidate this conception. Nor do the experimental results of Boyden,²⁹ Whitaker,³⁰ Higgins and Mann,³¹ Hamrick,³² Ivy and Oldberg³³ and others make it untenable. It has been shown by these authors that the gallbladder can be made to expel some of its content, and they have demonstrated the actual passage of certain opaque substances from the biliary vesicle into the duodenum. This, however, is far from proving that the gallbladder empties most of its content through the cystic duct under ordinary conditions or that its function is to do so. In an evaluation of experimental results of this kind, the possible anatomic variations of the neck of the gallbladder, of the cystic duct, and in man, also, particularly of the folds of Heister,³⁴ must be taken into account.³⁵ These structures, as will be shown later, are the ones entrusted with the control of the passage of bile toward the gallbladder. Their arrangement is such as to indicate that their function is to regulate the inflow and to hinder or prevent the outflow.

MECHANISM OF GALLBLADDER

The mechanism of the flow of bile into the gallbladder may perhaps be considered first. Coming from the hepatic ducts into the ductus choledochus, the bile may, of course, flow via the cystic duct into the gallbladder or through the opening of the papilla of Vater into the duodenum.³⁶ It is known that the outlet into the duodenum is only periodically open, whereas the passage toward the gallbladder is always

open. However, the bile has to make its way through a twisted tube which has a system of spiral-like folds narrowing its lumen. What is the force that drives the bile through the narrow cystic duct into the gallbladder in spite of the alternately arranged protruding folds of Heister?

Through a hole in the gallbladder wall caused by a needle-prick, bile escapes abundantly, indicating pressure within. As soon as the cystic duct is ligated, the flow decreases, showing that the pressure is more likely due to hydrostatic pressure within the bile ducts than to tension of the gallbladder wall, the contraction of which would tend to close the opening and stop the flow. In a pipet connected with the cannulated ductus choledochus of an anesthetized rabbit, the bile column may be observed to move forward only during inspiration. From this, it appears as if the pressure exerted on the liver during inspiration might be the force driving the bile into the gallbladder. When the entrance into the duodenum is closed, the bile ducts and the gallbladder form a Y-shaped communicating vessel of which the ductus choledochus is the stem, the common hepatic duct the one branch, and the cystic duct the other (fig. 1). The roots of the hepatic ducts being filled with bile high up to the smallest intrahepatic bile ducts, the fluid when pressed on will escape through the cystic duct into the gallbladder. It seems, then, as if the muscular coat of the gallbladder, the curves of its neck and the narrow cystic duct with the complicated folds of Heister were arrangements that compensate for pressure changes in the hepatic ducts.

It is in accordance with this that bile or any other fluid, injected with a slight pressure into one of the bile ducts, at any place above the duodenal portion of the ductus choledochus, first fills up the hepatic ducts and the ductus choledochus and then the cystic duct and the gallbladder. Before the gallbladder becomes much distended, the fluid enters the duodenum. But if there is a hole in one of the bile ducts, the injection of the gallbladder from the ducts does not succeed: the fluid passes through the hole, and neither the gallbladder nor the duodenum receives any. This is true for man or for animals tested, alive or dead.

From these experiments, simple as they are, it is safe to conclude that when the duodenal end of the ductus choledochus is closed, pressure, perhaps that exerted on the liver during inspiration, forces the bile into the gallbladder. The anatomic arrangement of the cystic duct with its heisterian folds and the curves of the neck of the gallbladder regulate the inflow of bile, whereas the muscular coat of the gallbladder prevents overdistention and produces adjustment in size at all times to the varying content. The latter statement, i. e., that the chief function of the muscular coat of the gallbladder is to prevent overdistention and to produce adjustment in size to the varying content and not, as is generally held, the emptying of the viscus, needs further elaboration.

If fluid is injected into the gallbladder with a syringe, the viscus first stretches to its maximum capacity, and while the resistance of the heisterian folds is successively overcome, one by one, the fluid passes through the cystic duct. Any surgeon or pathologist of experience can tell how difficult it frequently is to squeeze bile out of the normal gallbladder: If at necropsy the biliary vesicle is removed and freed of its

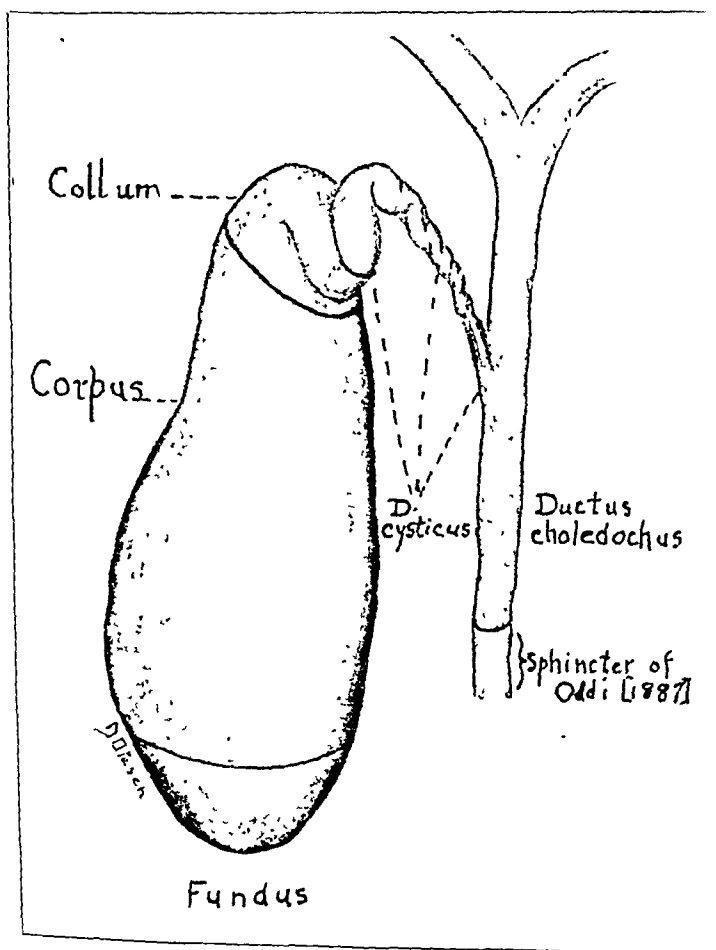


Fig. 1—Diagram of the extrahepatic bile ducts and the gallbladder. They form a Y-shaped communicating vessel of which the ductus choledochus is the stem, the common hepatic duct the one branch and the cystic duct the other.

content by cutting open the fundus, the heisterian folds usually prove "competent to the water test." The first fold of Heister, which marks the commencement of the neck of the gallbladder, is usually a high (about 7 mm.), thin, semilunar membrane which narrows the lumen to less than a third of the original diameter (fig. 2). The orifice is

eccentrically situated and leads into the upper limb of the S-shaped turn of the neck. At the lower limb of the S-shaped turn, a second fold narrows the lumen. Here the neck continues into the cystic duct, which tapers gradually toward its junction with the common hepatic duct (fig. 3). The crescent-like folds protruding into the lumen of the cystic duct are apparently arranged in a fashion to act as a system of "one way valves": they permit the inflow but prevent or hinder the outflow of bile from the gallbladder. The topographic relations and the structure of the gallbladder lend further support to this idea: the longitudinal axis of the gallbladder runs nearly parallel to the vertebral column; the tip of the fundus is lowermost and lies usually on a lower

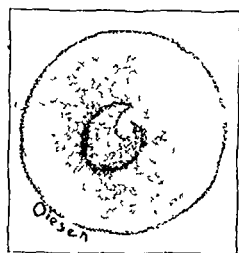


Fig. 2—The first fold of Heister. The commencement of the neck of the gallbladder is marked by the first fold of Heister, which is a thin semilunar membrane narrowing the lumen to less than a third of its original diameter. The orifice is eccentrically situated (drawing of a specimen of Dr. Sweet).



Fig. 3—Heister's illustrations of the neck of the gallbladder and the cystic duct. They show that Heister's conception of the anatomy of these structures was clear.

level than the papilla of Vater; furthermore, half of the surface of the body of the gallbladder is attached to the liver. Under these conditions the muscular coat would have to empty the gallbladder against the hydrostatic pressure of its own content, as well as force the bile through a small opening against the resistance offered by the curves and folds of the neck and the cystic duct.

The actual strength and arrangement of the muscular coat of the gallbladder, the history of its development and its behavior when it hypertrophies under stress are all in favor of the assumption that emptying of the viscus is not the function of the muscular coat. Genetically, the muscular coat of the gallbladder is probably a muscularis mucosae.

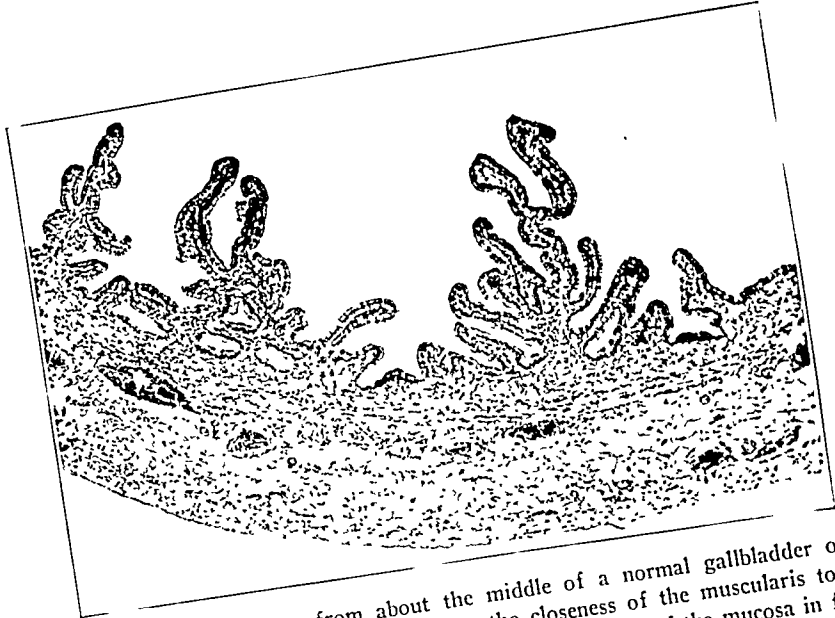


Fig. 4.—Cross-section from about the middle of a normal gallbladder of a 33 year old woman; $\times 40$. It illustrates the closeness of the muscularis to the lining epithelium, the absence of a submucosa, the richness of the mucosa in folds and the absence of glands.

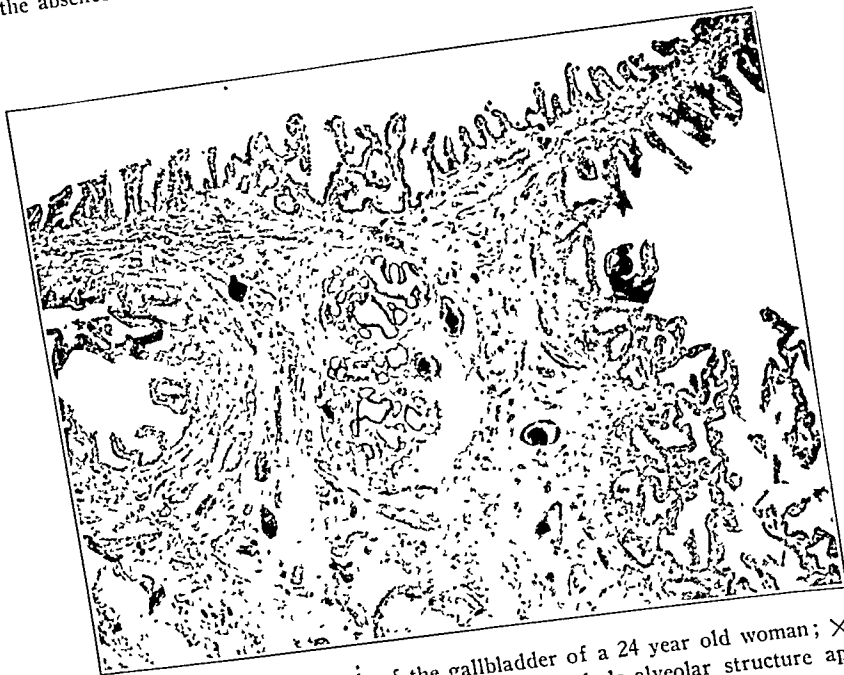


Fig. 5.—Glands in the neck of the gallbladder of a 24 year old woman; $\times 30$. In this cross-section, glands of an alveolar or tubulo-alveolar structure appear beneath the muscular coat, just as Brunner's glands, which penetrate the muscularis mucosae and lie in the submucosa.

In favor of this view are: the absence of a submucosa, the closeness of the muscularis to the lining epithelium (fig. 4), its comparatively late appearance in the development and also the fact that some of the glands occurring in the neck of the gallbladder penetrate the muscularis just as Brunner's glands perforate the muscularis mucosae of the duodenum³⁷ (fig. 5). The thickness of the muscularis varies considerably in different gallbladders and also in different parts of the same gallbladder. Usually there is a gradual but definite decrease toward the fundus and a slight increase toward the neck (figs. 6 and 7). Approaching the first

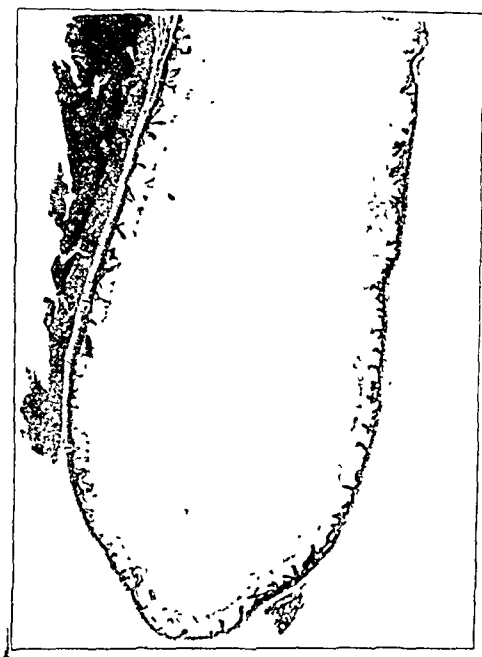


Fig. 6.—Longitudinal section of the distal half of the gallbladder of a female infant 38 days old; $\times 5$. The muscular coat is thinner about the fundus than in the middle portion.

heisterian fold the muscular coat becomes thinner, and the arrangement into inner, rather longitudinal and outer circular or oblique bundles seems to become disorganized. The bands of muscle fibers about the base of the heisterian folds and curves of the neck were interpreted by Lütken's¹ as a "collum-cysticus sphincter," which of course does not exist.

It should be added to all this that in some animals a contraction capable of bringing the mucosa of opposite sides into contact with one another is altogether impossible because of the structure or the topography of the gallbladder. In the two-toed sloth (*Choloepus hoff-*

*manni*³⁶), for example, on that side of the gallbladder which is attached to the liver the muscularis is missing in some places and scant in others as compared with the relatively large amount of musculature on the peritoneal side, which, however, comprises only one third of the circumference of the viscus (fig. 8). In most *rhesus* monkeys about two thirds of the entire surface of the gallbladder is embedded in the liver (figs. 9 to 11).

The cat's gallbladder is often of a peculiar shape, having two or more fundi, some of which may be lodged deep in the substance of the liver. In Boyden's³⁹ series of more than 2,500 cats, one in eight



Fig. 7—Longitudinal section of the fundus of the gallbladder of a 57 year old woman; $\times 5$. The muscular coat is hypertrophied and is thinnest about the dome of the fundus. The mucosa is seen to dip down between the muscle bundles forming deep outpouchings toward the external layers of the gallbladder: "Rokitansky-Aschoff sinuses" (see fig. 17). This gallbladder contained a number of "mixed gallstones." The size and shape of the viscus was about normal; the wall, however, appeared thickened. Microscopically, a cellular infiltration was noted in the subepithelial layer, in the intermuscular septums and to a lesser degree, also, in the perimuscular layer. The muscularis, which is hypertrophied, appears somewhat edematous. A slight edema is noted also in the rest of the layers, especially in the perimuscularis.

possessed some form of accessory gallbladder (fig. 12). Each of two lions that I had an opportunity of examining had bilobed gallbladders.³⁷ In the dog the lobes of the liver surrounding the free surface of the

gallbladder, are modeled to the shape of the viscus. Instances are known in which the gallbladder is totally embedded in the liver; in these cases, of course, an emptying contraction of the viscus is, *a priori*, utterly impossible. I have two specimens of this kind, one from a rhesus monkey (fig. 13) and one from a pig (fig. 14). The fact that these gallbladders could not empty their content through the cystic duct apparently did not interfere with their normal function; both contained no concretions or showed any demonstrable pathologic change. Data thus far obtained by studying the spontaneous contractions of the isolated gallbladder of the dog also indicate that the function of the muscular coat is that of preventing overdistention and of effecting adjustment in size to the varying content. Experiments performed

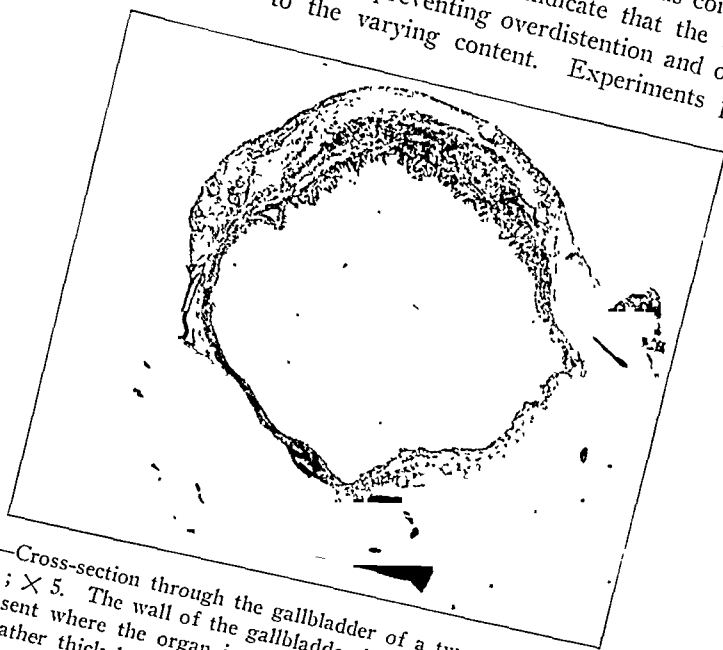


Fig. 8.—Cross-section through the gallbladder of a two-toed sloth (*Choloepus hoffmanni*); $\times 5$. The wall of the gallbladder is thinner and the muscle bundles scant or absent where the organ is attached to the liver. On the opposite side there is a rather thick layer of muscle bundles, but only to an extent of about one third of the circumference of the viscus.

together with Dr. Julian H. Lewis⁴⁰ were carried out in the following manner: The content of the freshly removed gallbladder was replaced with Locke's solution after thorough rinsing of the mucosa. The organ was then placed in an oxygenated bath of Locke's solution at body temperature. A specially constructed glass cannula tied into the neck of the gallbladder permitted accurate estimation of the fluid introduced into the viscus and, by its connection with a writing tambour, the registration of any change in the inner volume. Rhythmic contractions usually commenced soon after proper adjustments were made. They

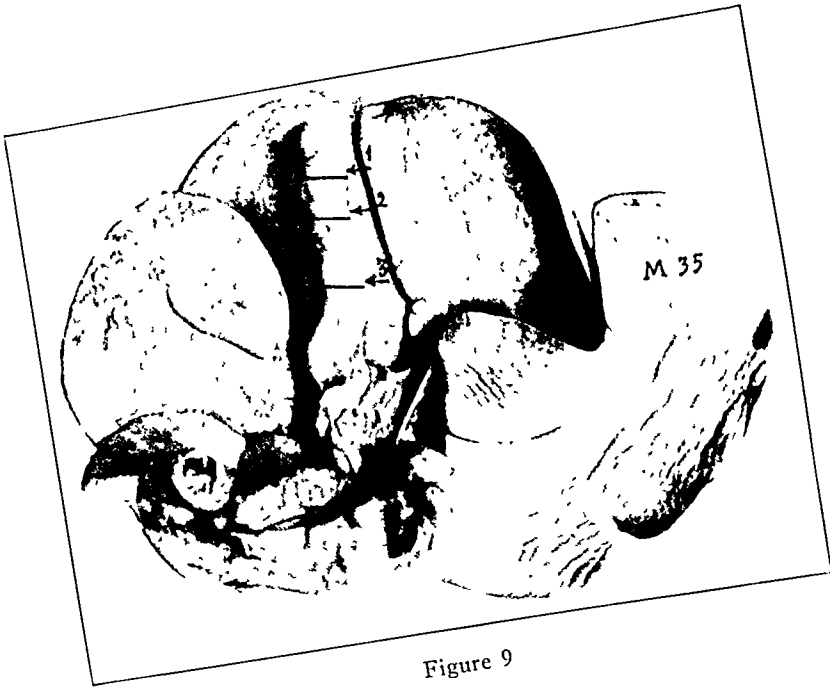


Figure 9

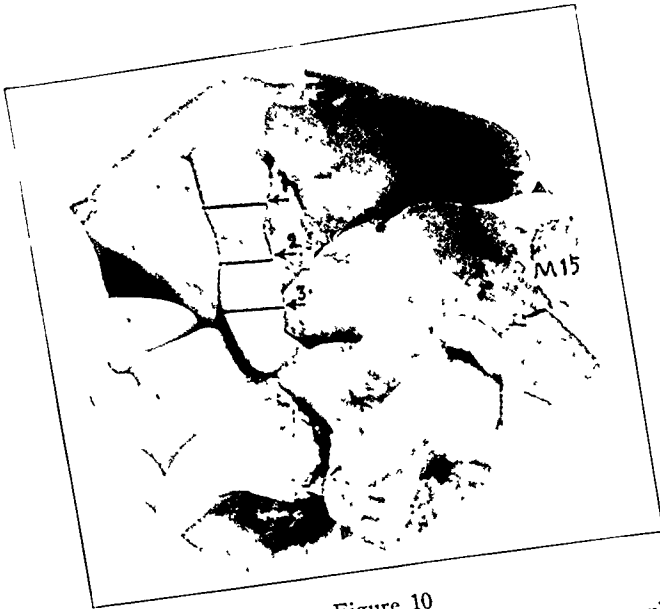


Figure 10

Figs. 9 and 10—Topography of the gallbladder in the rhesus monkey (*Macaca mulatta*). The tip of the fundus of the gallbladder does not reach the inferior margin of the liver but is embedded in the liver. The border of the fossa vesicae thins out gradually so that the gallbladder is framed in the liver like a gem set in a ring.

were usually from 2 to 46 mm. high, equivalent to the displacement of from 0.1 to 2.3 cc. of Locke's solution, and appeared at a rate of about 1 to 3 per minute. It was found that when the fluid content of the viscus was raised or lowered a change was registered, but soon adjustment occurred and the curve returned to the previous level and resumed its former shape (fig. 15).

It is known that the muscular coat of the gallbladder hypertrophies under stress. On such gallbladders dilatation of the cystic duct, exaggeration of the curves of the neck and the "relative insufficiency" of the heisterian folds are constant and conspicuous (fig. 16), but it is the

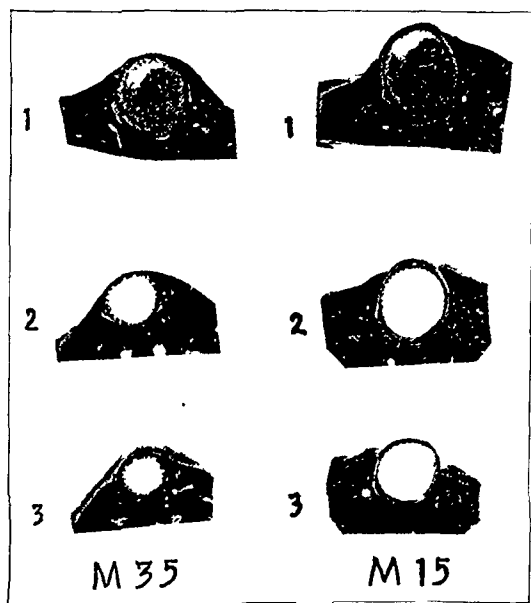


Fig. 11.—Transverse sections of the same gallbladders at levels marked are shown, illustrating that from two thirds to four fifths of the entire surface of the gallbladder is embedded in the liver.

presence of numerous hernia-like outpouchings of the gallbladder mucosa, the "Rokitansky-Aschoff sinuses,"⁴¹ which really tell the story. These outpouchings of the mucosa penetrate the muscular coat and appear with their dilated fundi in the perimuscular layer (figs. 17 and 18). It is evident that extreme contractions following prolonged and repeated overdistentions of the viscus lead to their formation: overdistention because it increases the size and possibly also the number of potential holes in the web of the muscularis, and extreme contractions, because as the viscus diminishes in size and the mucosa adapts itself to a smaller area of attachment the mucosa may be forced in some places

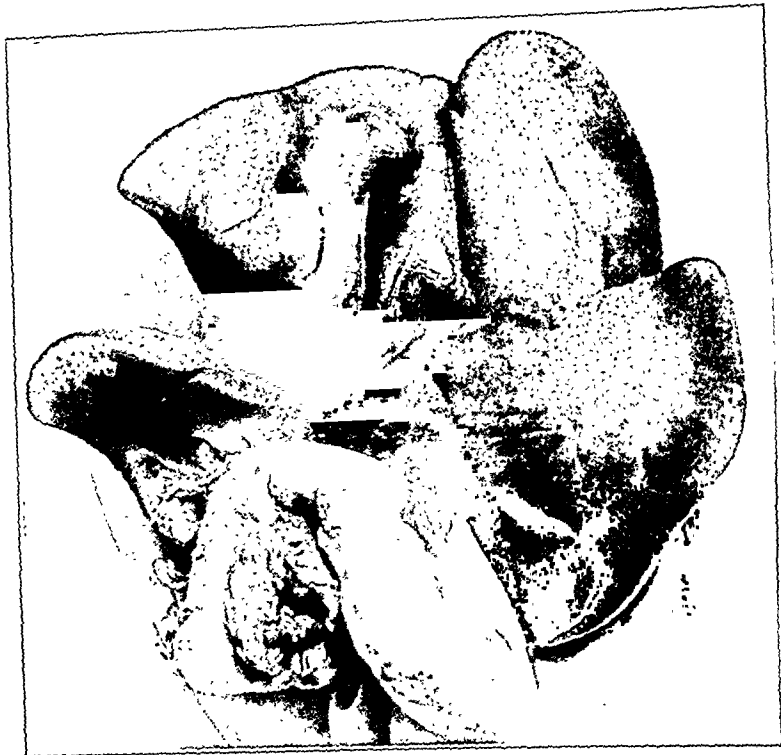


Fig. 12.—Trilobed gallbladder of a rhesus monkey.



Fig. 13.—Gallbladder of a rhesus monkey, embedded in the liver.

to dip down between the muscle bundles and protrude toward the external layers.⁴² Evidently, then, the process which calls for a hypertrophy of the muscular coat of the gallbladder leads also to the formation of hernia-like outpouchings of the mucosa which because they penetrate the muscular coat, certainly do not favor an effective contraction which would completely obliterate the lumen of the viscus (fig. 7).

EXPERIMENTS

An incidental observation made in Dr. Petroff's laboratory in the Trudeau Sanatorium gave new impetus to the search for conclusive evidence for or against the new hypothesis of the function of the gall-

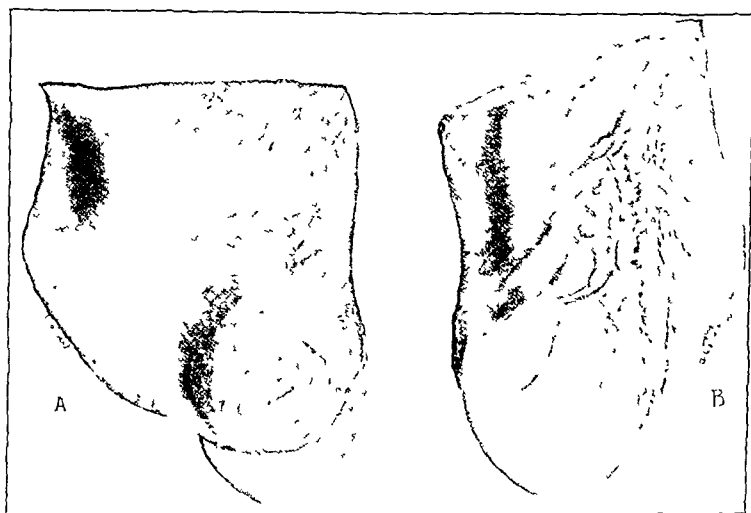


Fig. 14.—Gallbladder of a pig, embedded in the liver *A* is an anterior, *B* a posterior, view.

bladder. Dr. Petroff treated his colony of *rhesus* monkeys, affected with intestinal parasites, orally with methylene blue (methylthionine chloride, U. S. P.). At necropsy of one of these monkeys several days after the last dose, methylene blue was discovered in the gallbladder. Thus methylene blue seemed a promising agent for determining the correctness of the hypothesis that the bile which once has entered the gallbladder does not, under ordinary conditions, leave it again through the cystic duct. Experiments were carried out on rabbits after a method had been found for the quantitative determination of methylene blue and its leukoform in bile.⁴³ In one series the methylene blue was given intravenously and in another by stomach tube, in doses of 20 mg. per kilogram of body weight, that is, 2 cc. of a 1 per cent solution.

HALPERT—GALLBLADDER

It was found that in the rabbit anesthetized with ether the methylene blue appeared in the bile collected from the cannulated ductus choledochus within a few minutes after intravenous injection of the dye and reached highest concentration within less than one hour. This concentration of from 1:1,100 to 1:3,300 was approximately maintained for an hour or two. Then, dropping gradually, it showed from a fifth to a fifteenth of the highest concentration by the end of the sixth hour, the values ranging between 1:9,000 and 1:36,000. The bile removed from the gallbladder at the same time, i. e., six hours after the injection,

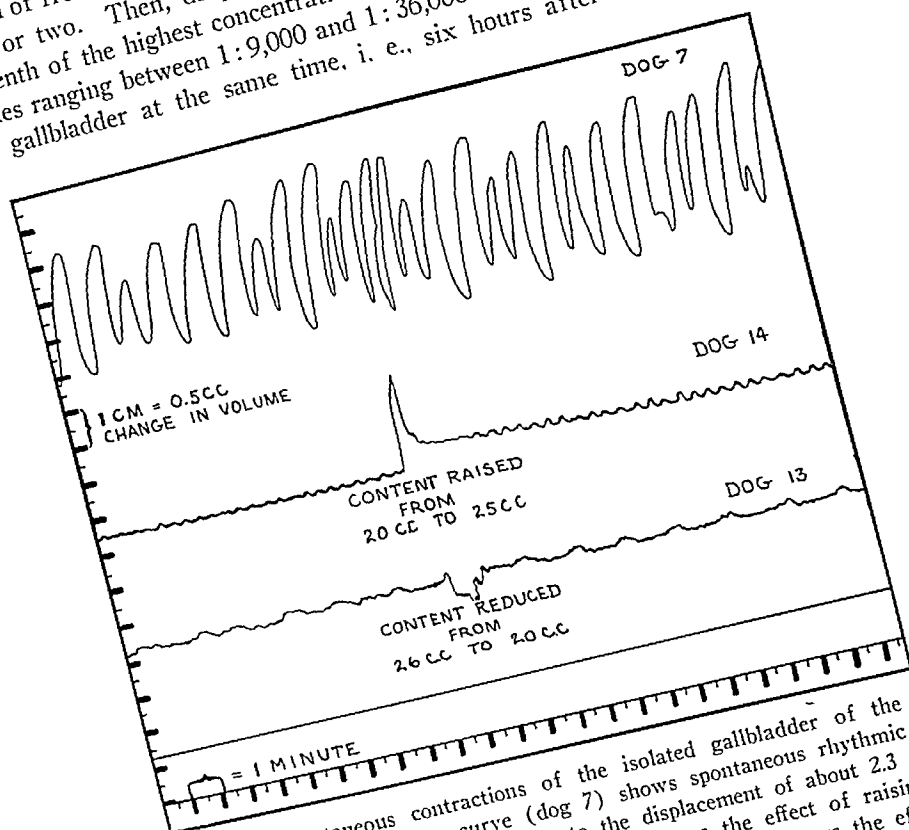


Fig. 15—Spontaneous contractions of the isolated gallbladder of the dog (Halpert-Lewis). The upper curve (dog 7) shows spontaneous rhythmic contractions as high as 46 mm., equivalent to the displacement of about 2.3 cc. of Locke's solution. The middle curve (dog 14) shows the effect of raising the fluid content from 20 to 25 cc. The lower curve (dog 13) shows the effect of reducing the fluid content from 26 to 20 cc. The middle and the lower curves illustrate that when the fluid content of the gallbladder is raised or lowered a change is registered, but soon adjustment occurs and the curve returns to the previous level and resumes its former shape.

usually contained from two to twenty-two times as much methylene blue as that contained in the last specimen of bile obtained from the ductus choledochus. Not only that, but at times, the concentration of methylene blue in the bile removed from the gallbladder was much higher—1:720

and 1:800—than the highest concentration ever reached in the bile collected from the ductus choledochus. This observation was the more remarkable since the gallbladder was never empty to begin with and since during the entire period of the experiment bile was passing freely through the cannulated ductus choledochus at a rate of from 5.5 to 13 cc. per hour.

In explaining these observations, it was necessary to assume either that bile had passed through the cystic duct into the gallbladder irrespective of the cannula in the ductus choledochus and that in the biliary



Fig. 16.—The neck of a hydrotic gallbladder of a 35 year old woman. The neck and the cystic duct are divided by a longitudinal section. The curves of the neck are exaggerated and the cystic duct is dilated to about ten times its original diameter. The gallbladder measured about 20 cm. in the longitudinal and 7 in the transverse diameter. It was filled with a viscid opaque fluid (white bile) and contained several "mixed gallstones," some of which were faceted.

vesicle a rapid concentration of the dye had taken place, or that the main bulk of the methylene blue reached the gallbladder by way of the blood stream and was excreted by its mucous membrane. Mann's experiments with rose bengal supported the latter assumption.⁴⁴ In order to clear the situation, in two rabbits the cystic duct was ligated, with particular care not to interfere with the circulation, the usual

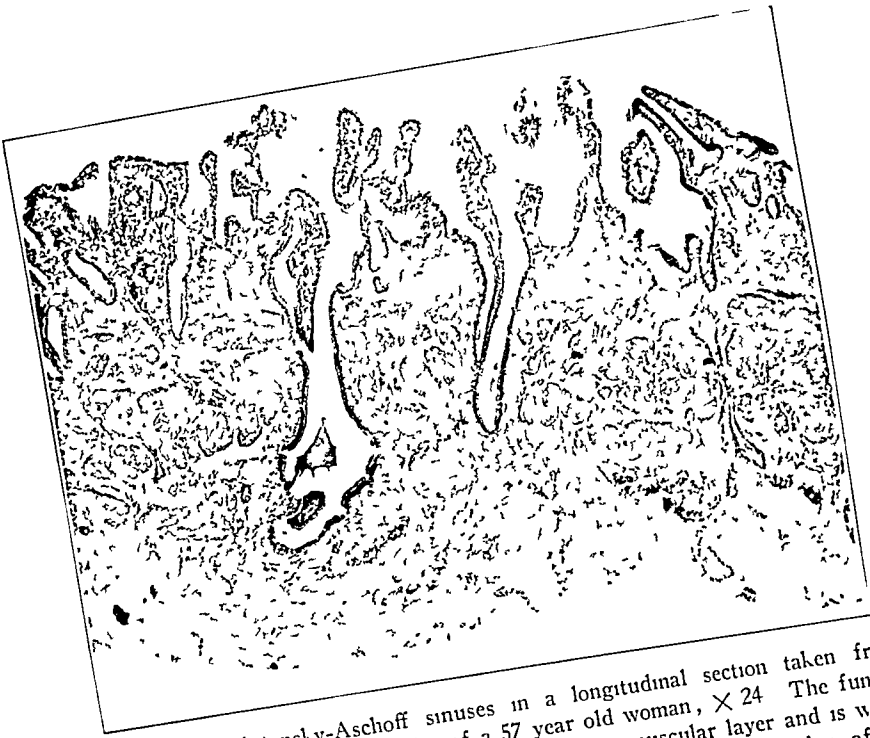


Fig 17—Rokitansky-Aschoff sinuses in a longitudinal section taken from about the middle of the gallbladder of a 57 year old woman, $\times 24$ The fundus of one of the two outpouchings is situated in the perimuscular layer and is wider than the part connecting it with the lumen of the gallbladder (section of the same gallbladder as fig 7)

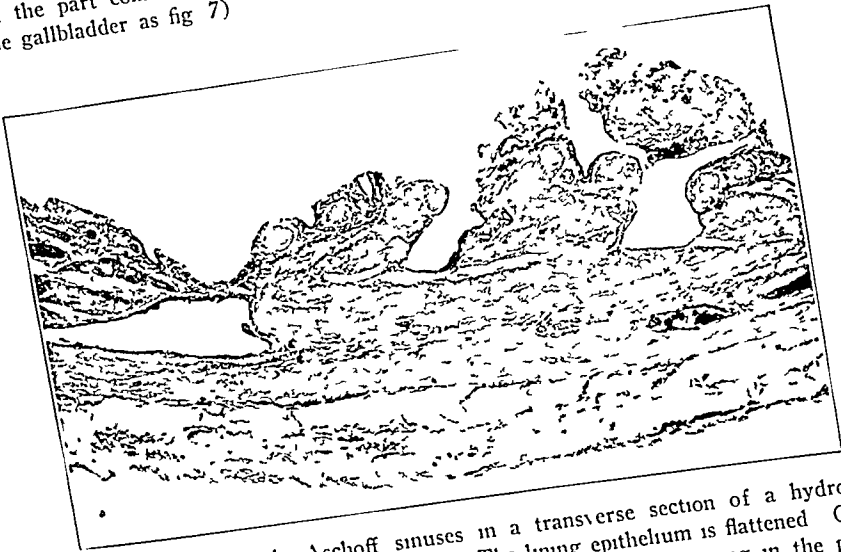


Fig 18—Rokitansky-Aschoff sinuses in a transverse section of a hydropic gallbladder of a 50 year old man, $\times 32$ The lining epithelium is flattened. Outpouchings of the mucosa bulge into the muscularis, one appearing in the perimuscularis. The muscular coat is hypertrophied—the arrangement of the muscle bundles into inner longitudinal and outer rather oblique or circular bundles is distinct. This gallbladder was filled with "white bile" and contained numerous "mixed gallstones" of various shapes and sizes

amount of methylene blue injected intravenously and the bile removed from the gallbladder two hours later. The estimated content of the biliary vesicle was about 2 or 3 cc. at the time of the ligation and injection. About two hours later less than 0.2 cc. of bile could be obtained from the gallbladder, which contained a hardly determinable trace of methylene blue. Obviously, then, the gallbladder mucosa was not excreting the dye. In other words, the methylene blue found in the gallbladder must have entered the viscus via the cystic duct.

In another series of experiments, the methylene blue was given by stomach tube in exactly the same amounts as in the experiments with injections. After the administration of the dye the animals remained in their usual environment and on their usual diet until the time of operation, particular care being taken that there was always food in their cages. The operation was performed at certain stipulated intervals between the twelfth and seventy-second hour after the ingestion of the dye in order to allow time enough for the action of any physiologic process which would tend to free the gallbladder from its methylene blue content.

It was found that bile collected from the cannulated ductus choledochus twelve, eighteen, twenty-four, thirty and thirty-six hours after the administration of methylene blue by stomach tube contained little if any methylene blue. On the other hand, bile removed from the gallbladder at the same time invariably contained the dye. Bile collected from the cannulated ductus choledochus forty-two, forty-eight, sixty and seventy-two hours after the administration of methylene blue by stomach tube did not contain methylene blue. On the other hand, bile removed from the gallbladder contained the dye even after seventy-two hours in most instances.

In these feeding experiments, the methylene blue was introduced through a catheter into the stomach; consequently, the greater bulk of the dye which reached the liver must have come there by way of the portal vein. I have no information as to how soon and in what initial concentration methylene blue appears in the bile after oral administration and how long it takes to reach the highest concentration and what this highest concentration is. But I learned that in none of the thirty-four animals whose gallbladders were opened between the twelfth and the thirty-sixth hours after feeding the dye did the bile collected from the ductus choledochus contain methylene blue in a higher concentration than 1:23,000; as a matter of fact, in fourteen the bile did not contain any methylene blue. Yet the bile in the gallbladder contained the dye in concentrations between 1:1,200 and 1:10,000 in nineteen of these animals and between 1:10,000 and 1:25,000 in eleven. The results in the forty-two, forty-eight, sixty and seventy-two hour groups of thirty-two animals are uniform. As mentioned before, in none of the animals

did the bile collected from the cannulated ductus choledochus contain any methylene blue. Yet at this time, in more than half of the cases, the bile in the gallbladder contained the dye in concentrations ranging between 1:4,850 and 1:26,000.

From the feeding experiments it was learned that ingested methylene blue appears in the bile and is excreted for some time, during which the pure bile in the gallbladder is gradually replaced by the dye containing bile. Since the gallbladder mucosa is apparently resorbing the dye less rapidly than it resorbs bile, the dye accumulates and stays there.

In addition to all that has been said, attention should be called also to the fact that the amount of bile delivered through the cannulated ductus choledochus during an experimental period of six hours averages about 10 cc. per hour, that is, the liver of a rabbit weighing 3 Kg. produces 240 cc. of bile per day, a conservative estimation. The average capacity of the gallbladder of the rabbit is about 3 cc. Furthermore, in the feeding experiments the animals were kept on their usual diet, and there was always food in their cages. Under these conditions, it is hard to conceive how methylene blue could remain in the gallbladder of an animal for a period of at least forty-two hours during which not less than 420 cc. of bile not containing the dye could have come from the liver, unless one gives up the idea that the function of the gallbladder is to empty and to refill. The tenacity with which the dye is retained in the biliary vesicle long after the liver has ceased to produce bile containing the dye is surely one of the strongest arguments favoring the assumption that bile does not leave the gallbladder through the cystic duct under ordinary conditions. This circumstance, of course, calls for a change in the current conception of stasis in the gallbladder.

If resorption is the principal function of the biliary vesicle, stagnation in the gallbladder may be due either to an abnormal composition of the bile or to a disturbed resorptive function of the gallbladder mucosa. The site of the process leading to stasis in the gallbladder may be, of course, in the liver or in the gallbladder, or in both the liver and the gallbladder.

If the stasis in the gallbladder is due to a disturbed or altered functioning of the liver, that is, if the gallbladder is intact but unable to remove by resorption all that is poured into it with the bile, one may speak of a hepatogenous stasis in the gallbladder. The experiments with methylene blue furnish a striking example of such a hepatogenous stasis in the gallbladder.⁴⁵ With the bile from the liver a substance, methylene blue, is poured into the gallbladder; the mucosa of the latter apparently cannot resorb the dye fast enough to cause its rapid disappearance, and so the dye stays there for days. It is evident that much the same thing happens when the sodium salt of tetraiodophenolphthal-

ein is administered for cholecystography. Both of these examples of hepatogenous stasis in the gallbladder support the idea that something of the same order happens in cases of marked cholesterolemia, when the cholesterol content of the bile is correspondingly exaggerated. Apparently because of the increased output of cholesterol by the liver, the mucosa of the gallbladder becomes, so to speak, saturated with the lipid substances which it has resorbed from the bile.⁴⁶ In such conditions, the cholesterol content of the bile in the gallbladder becomes greater and greater, and while the other bile constituents, those holding the cholesterol in solution, are being resorbed, the concentration finally may reach a point at which the cholesterol will crystallize out at the slightest provocation.

If the stasis in the gallbladder is caused by intrinsic functional disturbances or demonstrable pathologic conditions of the gallbladder itself, with the functioning of the liver more or less unimpaired, one may speak of a cystogenous stasis in the gallbladder. A variety of processes, such as acute, subacute and chronic inflammations, new growths, and the like, might lead to such a condition of the viscus.

CLASSIFICATION OF GALLSTONES

Perhaps the most convincing evidence for the existence of these two types, the hepatogenous and the cystogenous stasis, is furnished by the concretions usually found in these conditions. The chemical composition and the architecture of gallstones permit their ready classification into three groups.⁴⁷

Group I is the group of "pure gallstones," that is, those consisting purely or mainly of one of the stone-forming constituents of the bile, such as (a) cholesterol, (b) biliary pigments (calcium bilirubinate) and (c) calcium carbonate. For the formation of all of these so-called "pure gallstones," the liver is perhaps primarily responsible. At least stones of pure cholesterol usually occur in normal gallbladders the mucosa of which may show signs of resorption of cholesterol, and this is to be regarded as evidence of the attempt of the mucosa of the gallbladder to remove the excess of cholesterol in the content of the vesica fellea. Stones composed wholly of pigment, that is, those consisting of calcium bilirubinate, are believed to form in the finer intrahepatic biliary ducts. They might be found then, of course, in gallbladders that are shown microscopically to be intact. The small concretions of calcium carbonate also occur in gallbladders in which pathologic changes are not demonstrable. It is therefore reasonable to assume that some transient abnormal composition of the bile leads to their formation.

Group II is the group of the "mixed gallstones," that is, those consisting purely or mainly of at least two of the constituents of the "pure

gallstones." Here belong (a) the stones consisting of cholesterol and calcium carbonate, (b) the stones consisting of cholesterol and calcium bilirubinate, (c) the stones consisting of calcium bilirubinate and calcium carbonate T, and (d) the stones consisting of cholesterol, calcium bilirubinate and calcium carbonate. The formation of these, so-called "mixed gallstones," has generally been associated with infection. Infection and inflammation damage the mucosa of the gallbladder so that not all of the constituents of the bile are resorbed. Whatever physico-chemical explanation⁴⁵ is given for the process of formation of the "mixed gallstones" in inflamed gallbladders, the fact remains that the retention of the stone-forming constituents of the bile is due in the first place to a diseased condition of the gallbladder. Thus, "mixed gallstones" are formed in cystogenous stasis in the gallbladder, the stagnation being responsible for the formation of the stones and the infection for the stagnation.

It is evident that when a hepatogenous stasis in the gallbladder which has led to the formation of pure gallstones precedes a cystogenous stasis, "combined gallstones" form, which have a nucleus formed by one of the members of the group of "pure gallstones" and have a shell formed by one of the members of the group of "mixed gallstones." If, on the other hand, a cystogenous stasis in the gallbladder which has led to the formation of mixed gallstones is followed by a hepatogenous stasis, "combined gallstones" form, which have a nucleus formed by one of the members of the group of "mixed gallstones" and a shell formed by one of the members of the group of "pure gallstones."

The story of the formation of gallstones is then, briefly, as follows: A disturbed functioning of the gallbladder or an abnormal composition of the bile, or both, lead to a stagnation in the gallbladder of stone-forming constituents of the bile, the result of which is the formation of gallstones. The type of the concretion or concretions formed depends on the kind of biliary stasis which produced them. In a hepatogenous stasis in the gallbladder "pure gallstones" form, in a cystogenous stasis "mixed gallstones" form, and in an alternating stasis, "combined gallstones" form. Thus, gallstones can tell the story of the gallbladder; the story of a gallbladder, on the other hand, cannot be told unless its contents are known.

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FIBROMA OF THE VULVA CONTAINING AN EPITHELIAL INCLUSION CYST*

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BALTIMORE

Fibromas arising from the external genitalia in women are by no means common. In a study of 5,000 gynecologic cases tabulated at the Michigan University Hospital, in 1905, Burr¹ did not find a single case of vulvar fibroma. In 1917, Leonard² was able to find records of only six such tumors among the 23,000 patients admitted to the gynecologic department of the Johns Hopkins Hospital. Up to the present time, less than 175 fibromas of the vulva have been reported in all medical literature.

The majority of these growths arise in the *subcutaneous connective tissue*, but quite a large group of them originate in the *extraperitoneal portion* of the round ligament. It has long been known that the round ligament of the uterus, after traversing the entire length of the inguinal canal, emerges from the external inguinal ring and ends by breaking up into a number of diverging fibrous bands most of which become lost in the *subcutaneous tissue* of the labium majus, while a few find attachment to the pubic spine. In a certain number of cases of fibromas of the vulva, it is possible to feel a firm round cord running through the tumor, and, by following this cord upward, to trace it directly to one of these terminal fibers of the *extraperitoneal portion* of the round ligament, thus clearly demonstrating the point of origin of the growth. According to Leonard, as many as 33 per cent of these tumors arise in this manner.

There have been reported a moderate number of cases of fibrous tumors originating in the *subperitoneal connective tissue* and appearing at the vulva, and a few rare fibromas of the vulva have been supposed to arise in the connective tissue of the *rectovaginal septum* or of Bartholin's glands, or to have started in a hematoma. The tumors arising in the *subperitoneal connective tissue* and making their way to the vulva form an especially interesting group of neoplasms, because of the tremendous size attained by some of them. In 1905, Whitney and Harrington,³ published a comprehensive article on *subperitoneal fibro-*

* Submitted for publication, Nov. 22, 1928.

1. Burr, T. S.: Report of a Case of Fibroma of the Vulva, New York M. J. 81:340, 1905.

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3. Whitney, W. F., and Harrington, F. B.: Subperitoneal Pelvic Fibromata, Ann. Surg. 41:823, 1905.

mas based on the literature of nineteen such cases. Specifically, these subperitoneal tumors are supposed to arise from the connective tissue of the true pelvis, thus differing from the so-called retroperitoneal growths which originate in the root of the mesentery, the region of the kidney and the false pelvis.

In 1912, Aichel,⁴ reported a case of a fibrous tumor appearing at the vulva of an infant, and Esser⁵ and Polaillon⁶ each had a patient in whom a fibroma of the vulva arose after the menopause, but in the great majority of instances fibromas of the vulva have been noted in women in the child-bearing age. Many observers have for years commented on the periodic increase in size which these tumors undergo with each menstrual period, a phenomenon due to the increased blood supply to the vulva at that time. It has also been noticed that with each pregnancy there has usually been an increase in the rapidity of growth of the neoplasm.

When first seen, fibromas of the vulva usually appear as firm, smooth, round or oval nodules under the skin. As the growth increases in size, it may become pedunculated as a result of the constant pull of the tumor mass on the loose connective tissue in which it is embedded. When the patient is seen by the surgeon, there is often a definite pedicle, and the tumor presents a striking picture. The remarkable resemblance of some of these growths to a male scrotum has been noted frequently. The skin covering them is generally thick, and often between the menstrual periods it is thrown up into shallow folds. Both tumor and pedicle are frequently covered with hair. On palpation the tumors show the same firm consistence as fibromas elsewhere in the body, but if the circulation becomes impaired, they may become edematous and semifluctuant.

Fibromas of the vulva vary greatly in size, some of them remaining as small nodules while others grow to be tumors of enormous size. In 1851, Buckner⁷ reported a mammoth growth which arose in the subperitoneal connective tissue and appeared at the vulva. It is said to have weighed 268 pounds (121.5 Kg.) and is probably the largest human tumor ever reported. In the Warren Anatomical Museum at Harvard University,⁸ there is a daguerreotype made of this tumor while the patient was alive and also a detailed account of the history of the

4. Aichel: *Rhabdomyom des Ligamentum rontundum des neugeborenen Mädchens*, *Zentralbl. Gynäk.* **26**:57, 1912.

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8. Jackson, J. B.: *A Descriptive Catalogue of the Warren Anatomical Museum*, 1870, p. 642, no. 2982.

case and of the partial autopsy that was performed. As the abdominal viscera including the pelvic organs were all palpated through an opening made after death into the peritoneal cavity and found to be normal, there can be no doubt that the tumor arose extraperitoneally.

In 1917, Leonard, made an exhaustive study of all the recorded cases of fibromas of the vulva, giving in his article summaries of the gross and microscopic appearances in 100 cases that had been reported in the literature and reporting in detail the cases of six patients who had been treated in the Johns Hopkins Hospital. He showed that nearly one fifth of these tumors became sarcomatous. Hence, any sudden increase in rate of growth should be viewed with suspicion, and immediate surgical intervention is indicated.

Unless inflammatory or malignant changes occur, fibromas of the vulva produce few, if any, symptoms. If they are pedunculated they may cause some chafing of the skin with which they come in contact and thus interfere with locomotion. The large tumors may prevent coitus or become an obstacle at labor.

The diagnosis of fibromas of the vulva usually presents little difficulty. However, one must be careful not to mistake a tumor which originates in the extraperitoneal portion of the round ligament for a hernia. Nor should the possibility that these tumors may be adenomyomas instead of simple fibromas be forgotten. In 1896, Thomas Cullen⁹ first described adenomyoma of the round ligament and emphasized the diagnostic importance of severe pain associated with these tumors at each menstrual period. Although fibromas of the vulva are apt to become swollen at each period, they do not cause the patient any severe pain at that time for there is no hemorrhage into the tumor such as occurs in an adenomyoma every time menstruation occurs.

REPORT OF CASE

Recently, I happened to have under my care a patient with a fibroma of the vulva. A report of this case may be of interest for two reasons: First, the growth probably belonged to that group of less common fibromas of the vulva which originate in the extraperitoneal portion of the round ligament; secondly, the tumor contained a long, tubular, epidermoid sac. In this respect, I believe, it was unique, as a rather careful study of the literature failed to reveal another instance of a tumor of the vulva containing a similar structure. The following is a brief report of the case:

History.—Mrs. G. H., aged 33, seen on March 12, 1928, had always had good general health. Her appetite was fair. She had not had indigestion or nausea.

9. Cullen, T. S.: Adenomyoma of the Round Ligament, *Bull. Johns Hopkins Hosp.* 7:112, 1896.

The bowel movements had been regular, and she had not had any urinary symptoms. The menses had begun at 14 years; they had been regular and not associated with pain. There was no history of leukorrhea. The patient had been married for thirteen years and had had three children, now 12, 10 and 4 years of age. She had had considerable difficulty with each labor, but only with the first were instruments used. She had not had any miscarriages. Ten years before I saw her, when her second child was only 2 weeks old, she first noticed a small, hard lump in the right groin, which since that time had been gradually increasing in size. She thought that with each menstrual period there was a definite change in the tumor—that as the period approached it became larger and softer and after the period smaller and firmer. However, she had never suffered any pain referable to it at the time of the menstrual period. Six weeks before the patient entered the hospital, while she was bending over, the tumor became caught between two metal objects and she, being unaware of this mishap, straightened herself up, thus causing the entire tumor to be strongly pinched and severely traumatized. For several days the growth was red, tender and swollen, but under boric acid compresses the inflammation subsided. As the patient had not had any menstrual periods for six months, she considered herself to be six months' pregnant.

Examination.—On March 12, 1928, the general physical examination gave essentially negative results. The breasts contained colostrum. A symmetrical, firm tumor could be felt arising from the pelvis and extending 1 fingerbreadth above the umbilicus. As the fetal heart could be heard, there was no doubt that the uterus was pregnant. Arising from the right side of the vulva, immediately above the spine of the pubis, was a pedunculated tumor mass, measuring 15 cm. from its origin to its tip. Near its point of origin the tumor had a firm, constricted neck, but toward its lower portion it widened out until it had a diameter of 5 cm. It was covered with thin skin, suggesting that of a male scrotum. Only the upper part of the sac was covered with hair. There was a linear scar running along the tumor, in the center of which healing had occurred in such a way as to cause some invagination of the edges of the skin and to give the scar a dimpled appearance. This scar probably was caused by the injury two months previously.

On examination one could feel within the tumor a firm, circular band of tissue which extended from 3 cm. of the distal end to within 4 cm. of the point of origin of the tumor. As it stopped several centimeters from the point of origin of the tumor, it could not, of course, be traced up into the inguinal canal. This structure, while not attached to the overlying skin, felt as if it were in the outer part of the tumor rather than in its center. When the patient stood, the tumor hung down to within 8 cm. of the patella (fig. 1). There was no impulse over the femoral or the inguinal ring. The two sides of the vulva below the insertion of the tumor were exactly alike. With the patient lying on her back, careful examination showed that the tumor arose directly at the external inguinal ring (fig. 2). The internal pelvic examination showed the patient to have a moderately relaxed vaginal outlet and a soft cervix. The uterus was the size of a six months' pregnancy. The rectal examination and the urine showed nothing abnormal.

Operation.—At St. Joseph's Hospital, March 15, 1928, under local anesthesia, an oval incision was made around its base and the tumor removed. A few small vessels had to be ligated. The edges of the incision were approximated with chromic catgut and a small protective drain introduced. The drain was removed on the next day, and the patient had an uneventful convalescence.

The baby was born on June 15, 1928. The labor was uneventful. A final examination on July 8, 1928, did not show evidence of any return of the growth; the general condition was excellent.



Fig. 1.—The tumor reaches to within a short distance of the patella. The resemblance to a male scrotum is striking.

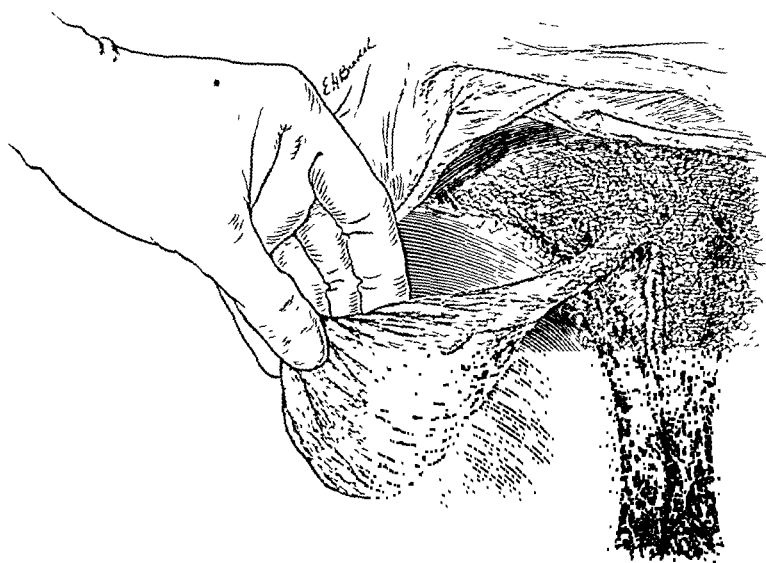


Fig. 2.—The tumor can be seen to arise directly over the external inguinal ring. The scar with a dimple in its center can be seen.

Pathologic Report (Johns Hopkins Hospital).—The specimen consisted of an elongated tumor, which was contracted at one end and somewhat dilated at the other. The entire tumor was covered with skin, and over its upper portion there was a moderate amount of hair. There was a healed scar in the skin over the tumor and in its center was a dimple. A firm, round cord could be palpated in the growth. This ran from within a short distance from the contracted end of the tumor almost all the way to the dilated end. When the tumor was split in half, the hemisections presented the firm white surface of fibroma.

The cordlike structure felt in the tumor stood out plainly (fig. 3). At the upper end of the tumor it seemed to fade into the skin, while at the lower end it

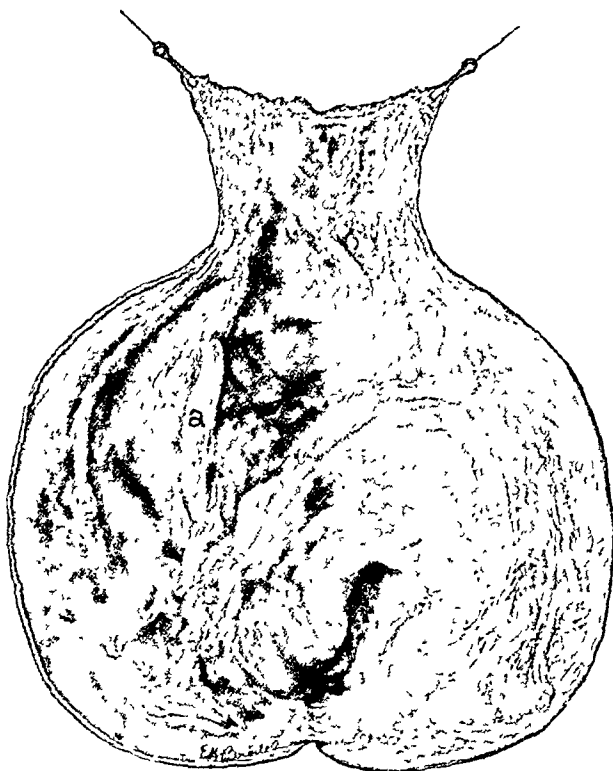


Fig. 3—The tumor split open. Some edema has developed in the lower dilated portion of the growth, which gives it a somewhat different appearance from the rest of the tumor. *a* marks the tube which was found in the tumor. Although not attached to the skin, this tube lies in the outer part of the tumor directly under the skin.

disappeared into the tumor itself. It was 6 cm. long and on cross-section showed a definite lumen which could be seen with the naked eye.

Microscopic sections taken from the tumor and the surrounding skin showed on the outside the normal squamous epithelium of the skin and below it the typical microscopic picture of a fibroma. The cordlike structure felt in the tumor was seen to be formed by a tube lined with several layers of squamous epithelium of

the same character as that of the skin on the outside of the tumor. The photomicrograph showed that this tube, while not attached to the skin, lay only a short distance below it (fig. 4). The tube had a lumen filled with debris, probably made up of desquamated epithelial cells. Some cornification of the internal layer of epithelium had occurred. There was a moderate accumulation of small round cells on the outside of this tube (fig. 5).

COMMENT

This fibroma of the vulva could not be traced directly into the inguinal canal. However, from the fact that it arose from a point

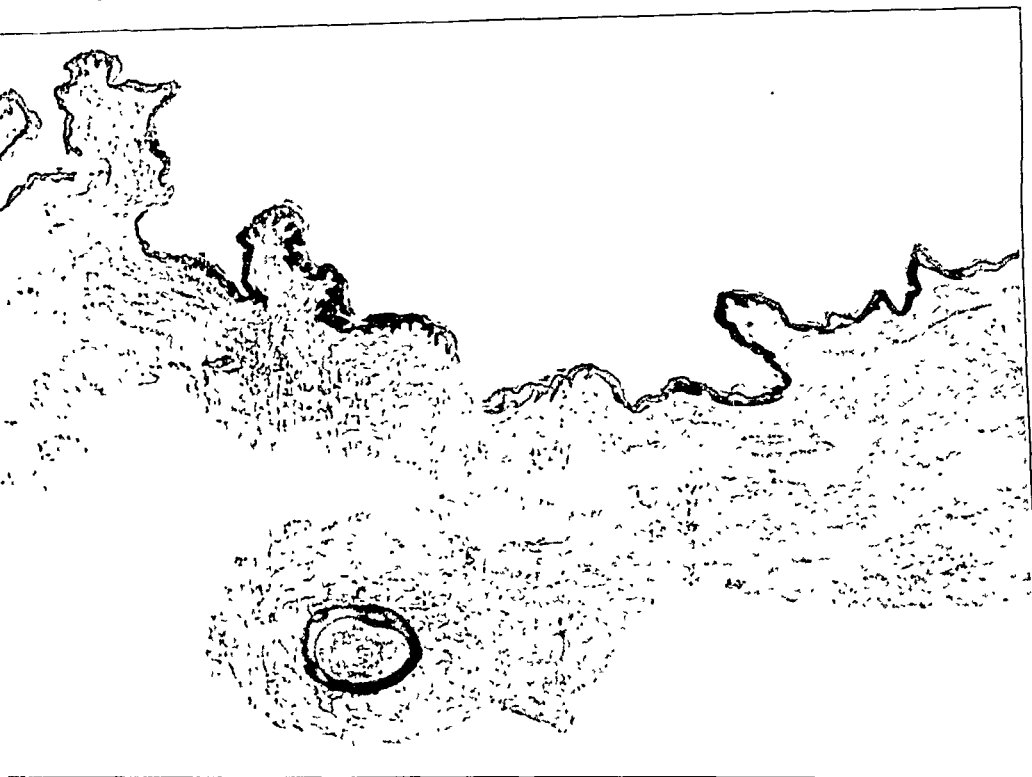


Fig. 4.—Photomicrographic appearance of the tumor. On the outside is the squamous epithelium of the skin. Below this is the fibroma. The tube lined with squamous epithelium lies directly under the skin.

directly over the external inguinal ring, just where the extraperitoneal portion of the round ligament breaks up into its terminal fibers, it seems more likely that this growth arose from one of these terminal fibers rather than from the fibrous elements found in the subcutaneous tissue.

It is difficult to find a satisfactory explanation for the occurrence of the tube with squamous epithelium that was found in this tumor. The tube was not the terminal portion of a hydrocele of the canal of Nuck,

for such a structure, being really a pouch of peritoneum, would have a lumen lined with cuboidal, columnar or flat epithelium and not with the squamous variety. There is nothing about this tube to suggest that it is a dermoid, nor does it resemble a hidradenoma, a definite type of neoplasm, first described by Pick¹⁰ in 1904 and supposed to arise from

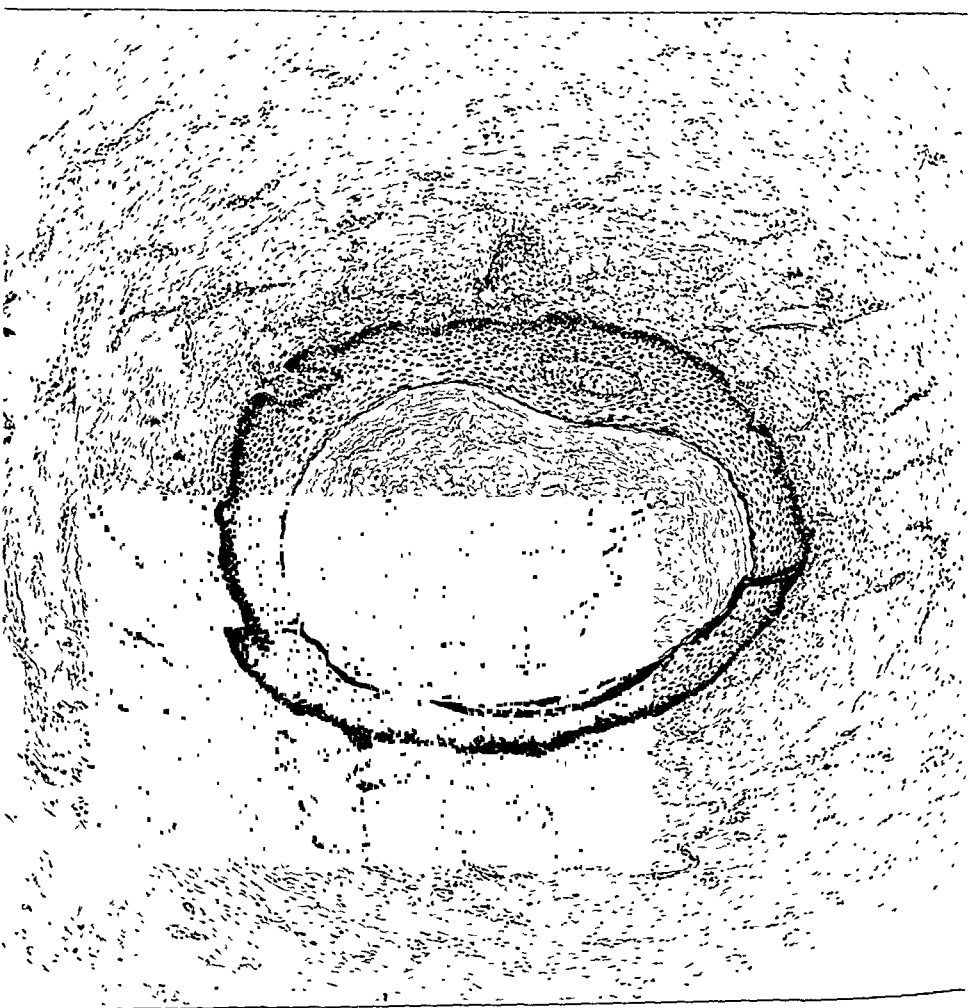


Fig. 5.—Photomicrographic appearance of the traumatic epithelial cyst or tube. The squamous epithelium is several layers deep. Some cornification of the internal layer of epithelium has occurred. The lumen of the tube is filled with debris. There is a moderate accumulation of small round cells on the outside of the tube.

10. Pick, Ludwig: Ueber Hidradenoma und Adenoma Hidradenoides, Virchows Arch. f. path. Anat. **175**:312, 1904.

the sweat glands of the vulva. Microscopically, hidradenomas suggest rather actively growing adenomas.

One theory for the occurrence of this epithelium lined tube in the fibroma is that as a result of trauma part of the outside skin was forced down into the tumor, and that this fragment of skin continued to grow and formed an epithelium lined tube in the tumor. This theory appears to be plausible because the tube was situated in the outer part of the tumor rather than in its center and was lined with squamous epithelium. Moreover, there was a definite history of the tumor being severely traumatized, and at this time part of the overlying skin may have been forced down into the tumor.

Although a careful search of the literature failed to reveal any other instances of a vulvar fibroma containing such a tube as was found in the case reported, quite a few instance of epidermoid inclusion cysts of the hand and fingers have been reported. As far back as 1855, Wernher¹¹ removed a tumor, which was probably of this nature, from the palm of a man's hand, but he considered it to be an atheroma. Many of the earlier investigators thought that these tumors developed from sweat glands, although this opinion necessitated the belief that glandular epithelium changed into squamous epithelium. However, in 1887, Franke¹² stated that quite a number of epithelial cysts of the skin previously reported had been wrongly called atheromas or dermoids, and for these cysts he proposed the name epidermoids. Even Franke, however, did not understand how these cysts are formed, since he spoke of them being of congenital origin, and it remained for Reverdin¹³ to explain their etiology. He observed that these cysts almost always developed after an injury, such as a stab, pinch, bite or crush, and collected reports of thirty cases of epidermoid cysts from the literature in all of which there was a history of trauma with a later development of an epidermoid cyst below the injured skin.

On the experimental side Kaufman,¹⁴ in 1884, and Gross,¹⁵ in 1885, proved that loose pieces of skin could be implanted in the subcutaneous tissue of animals as well as in the abdominal cavity, and that these pieces of skin would continue to carry out their physiologic function, namely, that of the production of epidermis. They found that after a short time the implanted epidermis developed into a cyst.

11. Wernher, A.: Das Atherome ein eingebolgtes Epitheliom, *Virchows Arch. f. path. Anat.* 8: 22, 1855.

12. Franke, F.: Ueber das Atherom besonders mit Bezug auf sein Entstehen (das Epidermoid), *Arch. f. klin. Chir.* 34: 507, 1887.

13. Reverdin, J. L.: Des kystes epidermiques des doigts, *Rev. med. de la Suisse Rom.* 7: 38, 1887.

14. Kaufman: Ueber Enkataraphie von Epithel, *Virchows Arch. f. path. Anat.* 97: 236, 1884.

15. Gross: Contribution a l'etude des tumeurs perlées, Paris, 1885.

Since the publication of these first articles on traumatic epithelial cysts of the hands, only occasional reports on this subject have appeared. In 1893, Bland Sutton¹⁶ reported the case of an implantation cyst on the thumb of a girl, aged 18 years. In 1895, Wörz¹⁷ reported three additional cases and summarized the literature on these tumors up to that time. During the last few years the best article on this subject was published in 1921 by Carossin,¹⁸ an Italian observer, who, in addition to covering thoroughly the entire subject and reviewing the literature, reported the case of a traumatic epithelial cyst occurring on the palmar surface of the middle finger.

Epidermoid inclusion cysts have been found in one other locality besides the hand and fingers, namely, the vagina. While for many years they have been occasionally found and reported here, it was not until 1899 that Stokes¹⁹ correctly explained their etiology. Previous to the publication of his article it had been noticed that cysts in the posterior vaginal wall occasionally followed traumas to the vagina, such as occur in perineal tears or when a perineal operation is performed, but he was the first to stress the point that these cysts developed only when some of the surface epithelium is included within the edges of the wound. It is easy to understand how in doing a perineorrhaphy a surgeon, in denuding the vaginal mucosa, might accidentally miss small bits of mucous membrane and then, in bringing the tissues together, bury these islands of vaginal mucosa deep down in the tissue where later they might develop into vaginal epidermoid cysts. In 1905, Thomas Cullen²⁰ showed that in twenty-four instances of epidermoid cysts occurring in the lower lateral or posterior vaginal wall, there was a history of a lacerated perineum and in five out of the twenty-four the perineal tear extended into the rectum.

Some recent experimental work performed on dogs by Davis and Traut²¹ is of special value to those interested in the formation of epithelium lined cysts. These investigators cut whole thickness grafts, placed them on one of the abdominal muscles from which the fascia had been stripped and sutured them in position under approximately the

16. Sutton, Bland: A Clinical Lecture on Some Unusual Tumors, *Brit. M. J.* **1**:461, 1895.

17. Wörz, A.: Ueber traumatische Epithelcysten, *Ztschr. f. klin. Chir.* **18**:753, 1897.

18. Carossin, G.: Le cisti epitheliali traumatiche del palmo dello mano, *Gior. di. med. ferrov. Prato.* **1**:20, 1921.

19. Stokes, J. E.: The Etiology and Structure of True Vaginal Cysts, *Johns Hopkins Hosp. Rep.* **7**:109, 1899.

20. Cullen, T. S.: Vaginal Cysts, *Bull. Johns Hopkins Hosp.* **16**:207, 1905.

21. Davis, J. S., and Traut, H. F.: The Production of Epithelial-Lined Tubes and Sacs, *J. A. M. A.* **86**:339 (Jan. 30) 1926.

tension under which they had been as parts of the external skin. The result of this procedure was the formation of either an epithelium lined cyst or a tube, according to the shape of the buried graft. The epithelium of the graft grew outward from the margins and completely covered the contiguous tissues. As the two margins met, either a tube or a sac was formed. Microscopic examination of cross-sections of these tubes or sacs showed not only that epithelium surrounded the lumen but that this was several cells deep and in a viable condition. In these experiments, Davis and Traut found it took about twenty days for the margins of the buried skin grafts to unite and form tubes. The maximum development of the epithelium lining the tubes was reached in forty days, after which it began to degenerate, probably as a result of the pressure exerted by the fluid secreted within the cyst.

In my case, the fibroma of the vulva had been severely pinched six weeks before operation. It seems possible that at that time an elongated strip of skin was forced down into the tumor and that the edges of this strip of skin continued to grow, united and formed an epithelium lined tube.

SUMMARY

A large fibroma of the vulva is recorded, which probably had originated from one of the terminal fibers of the extraperitoneal portion of the round ligament.

The tumor contained within it a tube lined with several layers of squamous epithelium. Its development is probably to be explained as follows: As the result of trauma (a severe pinch), a strip of skin was forced down into the tumor and the edges of the enclosed skin; it continued to grow, united and formed an epithelium lined tube.

EXPERIMENTAL ILEUS

I. HIGH OBSTRUCTION WITH THE BILIARY, PANCREATIC AND DUODENAL SECRETIONS SHORT-CIRCUITED BELOW THE OBSTRUCTED POINT*

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The cause of death in acute intestinal obstruction has not yet been definitely established. Most investigators are of the opinion that it is the result of absorption of a toxin in the obstructed bowel, which may be formed either in the mucosa of the bowel and absorbed directly¹ or in the lumen of the intestine as the result of the action of normal digestive secretions, abnormal or perverted secretions² or of bacteria³ on the stagnated contents of the obstructed bowel. The absorption of this toxic substance within the intestine is thought to be influenced by the degree of damage to the mucosa from distention,³ and by increased intraviscus pressure.⁴ It is believed by some that the toxic element can be isolated, and that it is a split protein product, which, when injected into normal animals, produces a severe toxemia and death.⁵ On the other hand, there are a few who feel that death is due to a marked disturbance of the water and mineral balance of the body from dehydration and loss of sodium and chloride ions.⁶ A thorough review and analysis of the experimental work on intestinal obstruction is given in Cooper's⁷ recent article.

To determine the rôle of the biliary, pancreatic and duodenal secretions in the rapid death from high intestinal obstruction, which usually occurs in from two to eight days in the dog,⁸ an experiment was devised

* Submitted for publication, May 31, 1929.

* From the Department of Surgery, the University of Chicago.

1. Whipple; Stone, and Bernheim: *J. Exper. Med.* **17**:307, 1913.

2. Ellis: *Ann. Surg.* **75**:429, 1922.

3. Murphy, F. T., and Brooks, B.: *Intestinal Obstruction*, *Arch. Int. Med.* **15**:392 (March) 1915. Dragstedt; Dragstedt; McClintock, and Chase: *J. Exper. Med.* **30**:109, 1919.

4. Stone, H. B., and Firor, W. M.: *Absorption in Intestinal Obstruction*, *Soc. Proc., J. A. M. A.* **84**:141 (Jan. 10) 1925. Owings; McIntosh; Stone, and Weinberg: *Intral Intestinal Pressure in Obstruction*, *Arch. Surg.* **17**:507 (Sept.) 1928. Stone: *Am. J. Surg.* **1**:282, 1926.

5. Whipple; Rodenbaugh, and Kilgore: *J. Exper. Med.* **23**:123, 1916.

6. McIver, M. A., and Gamble, J. L.: *Body Fluid Changes Due to Upper Intestinal Obstruction*, *J. A. M. A.* **91**:1589 (Nov. 24) 1928.

7. Cooper, H. S. F.: *Cause of Death in High Obstruction*, *Arch. Surg.* **17**:918 (Dec.) 1928.

8. Haden, R. L., and Orr, T. G.: *Obstruction of Jejunum: Effect on Sodium Chloride in Chemical Changes in Blood of Dogs*, *Arch. Surg.* **11**:859 (Dec.) 1925.

which permitted these three secretions to be short-circuited below the point of obstruction. This was done by operations in either two or three stages. Six dogs with obstruction produced in this way lived from twelve to thirty-three days.

EXPERIMENTAL WORK

Dog 337.—First Stage: After pylorectomy, the end of the duodenum was closed. The jejunum was sectioned about 8 cm. beyond the duodenum. The open end of the distal part was closed and then an end-to-side anastomosis was made between it and the open end of the stomach. The proximal part was anastomosed to the upper portion of the ileum by the end-to-side method. In this way the stomach drained into the jejunum, and the duodenum into the ileum.

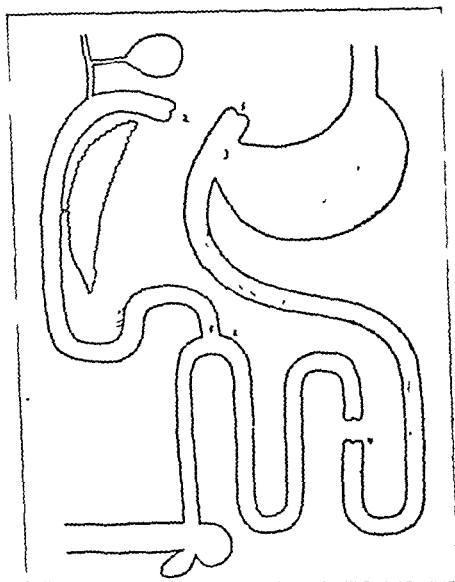


Fig. 1.—Two-stage procedure. First: pylorectomy, 2; section of the jejunum, 5, anastomosis of proximal part of jejunum to ileum, 1; anastomosis of distal part to stomach, 3; second: obstruction of the jejunum, 4.

Second Stage: Three weeks later, an obstruction was produced in the jejunum by sectioning the bowel 75 cm. from the stomach and closing the ends (fig. 1).

After obstruction was produced, the general condition of the dog was excellent. It walked and ran about normally, drank water freely, ate food sometimes, vomited occasionally and passed several small stools. On the sixteenth day it weakened markedly and death occurred on the seventeenth day. The weight gradually declined from 11.4 to 7.6 Kg., a total loss of 33 per cent, an average loss of 0.22 Kg. per day, or 1.95 per cent per day. The blood chemistry showed a fall in total chlorides estimated as sodium chloride from 525 to 395 mg. per hundred cubic centimeters. There was a rise in carbon dioxide capacity from 49 to 76, and in nonprotein nitrogen from 30 to 39 mg. per hundred cubic centimeters. There was little change in the content of urea nitrogen which varied from 14 to 15 mg. per hundred cubic centimeters (fig. 2). At autopsy, the abdominal cavity

was found filled with several ounces of gray, purulent fluid. About 18 cm. of the end of the bowel beyond the point of obstruction had undergone intussusception. This part was distended and discolored and contained a small area of gangrene with perforation. The stomach and the jejunum, which was anastomosed to it, were distended with a thick gray fluid. The lungs and other organs were grossly normal. Death was due to general peritonitis following intussusception and perforation of the bowel.

Dog 515.—First Stage: This stage was the same as for dog 337, except that the proximal part of the sectioned jejunum was anastomosed to the ileum by the side-to-side method after the open end had been closed.

Second Stage: Twelve days later, obstruction was produced by sectioning the jejunum 26 cm. from the stomach.

The general condition of the dog following obstruction was good until the ninth day, when it began to show signs of weakening, which progressed until its death

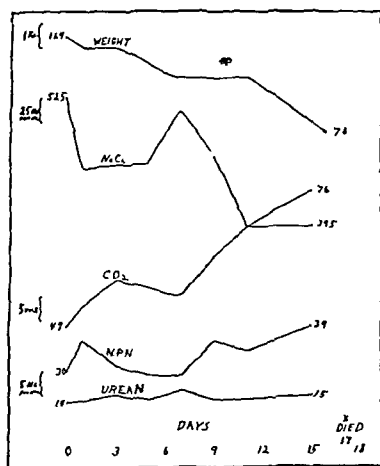


Figure 2

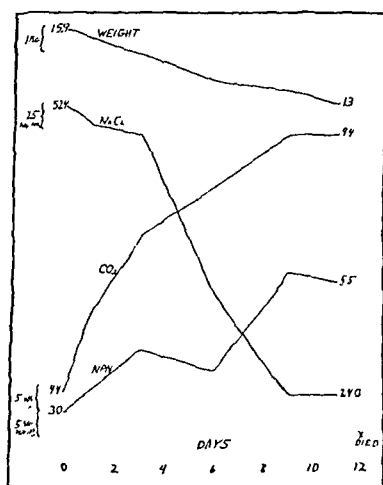


Figure 3

Fig. 2.—Weight and chemistry readings for dog 337; obstruction at 76 cm.; death on the seventeenth day.

Fig. 3.—Weight and chemistry readings for dog 515; obstruction at 26 cm.; death on the twelfth day.

on the twelfth day. Drinking, eating, vomiting and passage of stools occurred as in dog 337. The weight declined from 16 to 13 Kg., which was a loss of 19 per cent, an average of 0.27 Kg. or 1.7 per cent per day. The blood chemistry showed a fall in sodium chloride from 524 to 240, a rise in carbon dioxide capacity from 44 to 94 and in nonprotein nitrogen from 30 to 55 (fig. 3). At autopsy the stomach and jejunum down to the point of obstruction were distended. The remaining bowel was partially collapsed. The organs were grossly normal, except for consolidation in the lower lobe of the right lung. Death was due to bronchopneumonia.

Dog 983.—First Stage: A lateral anastomosis was made between the middle of the ileum and the jejunum just beyond the duodenum.

Second Stage: One week later, the pylorus was resected and the open ends of the stomach and duodenum were closed. An anterior gastro-enterostomy was made, the jejunum just beyond the lateral anastomosis being used. The proximal portion of the jejunum was sectioned between the two anastomoses, and the ends were closed.

Third Stage: Three weeks later, an obstruction was produced by sectioning the bowel above the entero-anastomosis, 150 cm. below the stomach (fig. 4).

The general behavior of the dog following obstruction was similar to that of the two animals described. Death occurred on the seventeenth day. The weight declined from 20.6 to 15 Kg., a total loss of 32 per cent and an average loss of 0.39 Kg. or 1.8 per cent per day. The blood chemistry showed a gradual fall in sodium chloride from 547 to 271 and a rise in carbon dioxide capacity from 44 to 78. The content of nonprotein nitrogen changed only slightly during the first two weeks,

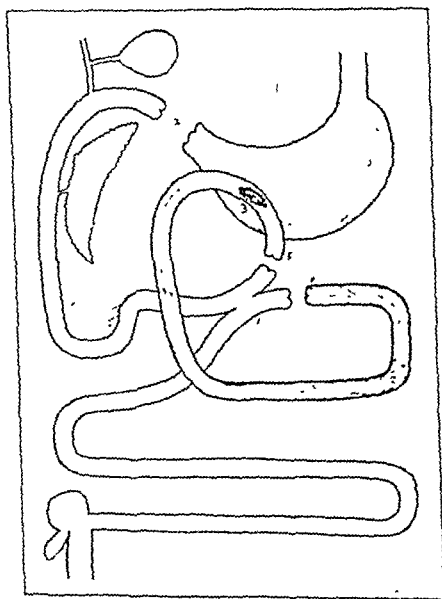


Fig. 4.—Three-stage procedure. First: (dogs 983, 493, 492 and 489) lateral anastomosis between upper part of jejunum and upper ileum. Second: (dog 983) pylorectomy, 2, anterior gastro-enterostomy, 3, and interruption of jejunum, 5; (dogs 493, 492 and 489) pylorectomy, 2, and anterior gastro-enterostomy. Third: (dog 983) obstruction of the bowel, 4; (dogs 493, 492 and 489) interruption of jejunum, 5, and obstruction of jejunum, 4.

but rose abruptly just before death to 127. The urea nitrogen also changed little, except for a terminal rise to 81 (fig. 5). Autopsy showed a dilatation of the terminal 15 cm. of the obstructed bowel without any marked change above this or in the stomach. The only other gross change was consolidation in the lower lobe of the right lung. The immediate cause of death was bronchopneumonia.

Dog 493.—First Stage: The procedure was the same as for dog 983, except that the upper part instead of the middle part of the ileum was used. The dog weighed 20.8 Kg.

Second Stage: The weight was 21.6 Kg. This stage was three weeks later and was the same as for dog 983, except that the jejunum was not sectioned between the two anastomoses.

Third Stage: The weight was 21.3 Kg. This stage was done two and a half weeks later and consisted of interruption of the upper jejunum between the entero-anastomosis and the gastro-enterostomy, and obstruction of the jejunum 90 cm. from the stomach (fig. 4).

The general behavior of the animal was not markedly changed following the obstruction, except that it appeared less lively. It was able to walk about all right until the twenty-fifth day, when it appeared to be growing weak. Weakness progressed during the next day, and death occurred on the morning of the twenty-seventh day. The daily intake of water by mouth was from 400 to 500 cc., to which about 1 Gm. of sodium chloride was added every third day, and dextrose

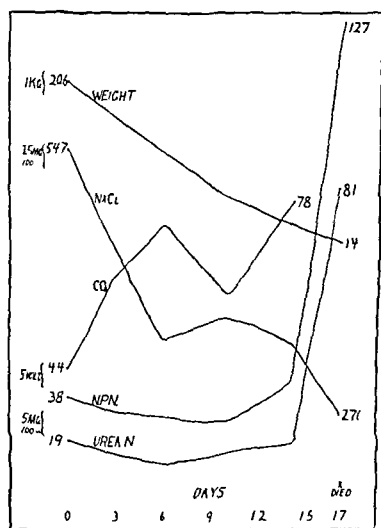


Figure 5

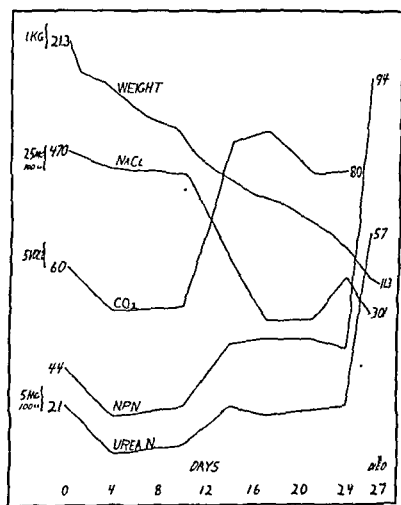


Figure 6

Fig. 5.—Weight and blood chemistry readings for dog 983; obstruction at 150 cm.; death on the seventeenth day.

Fig. 6.—Weight and blood chemistry readings for dog 493; obstruction at 90 cm.; death on the twenty-seventh day.

occasionally. Small feedings of meat were given about twice a week. Vomiting occurred only about twice a week. The urinary output was from 200 to 300 cc. per day. Small black or brown stools were passed on an average of two or three times a week. The weight gradually declined from 21.3 to 11.6 Kg., which was a loss of 45 per cent, an average of 0.37 Kg. or 1.75 per cent per day. The blood chemistry showed a fall in sodium chloride from 47.0 to 30.1 and a rise in carbon dioxide capacity from 59 to 80, in nonprotein nitrogen from 44 to 94, and in urea nitrogen from 21 to 57, the latter two making the most abrupt rise just before death. During the first ten days of the obstruction, the carbon dioxide and non-protein and urea nitrogen showed a moderate fall (fig. 6). Autopsy revealed a

marked dilatation of the stomach and of the obstructed loop of jejunum which was most marked in the lower third, where it measured from 4 to 5 cm. in diameter. In addition, there was an intussusception of the ileum, 15 cm. below the anastomosis with the jejunum, which had produced a complete obstruction at this point. This made a closed intestinal loop into which the pancreatic, biliary and duodenal secretions emptied. The loop was as markedly distended as the obstructed jejunum. Beyond this intussusception the bowel was only partially collapsed down to a second point where another telescoping had occurred. Beyond this point it was completely collapsed (fig. 7). The stomach contained 200 cc. of a thick gray material and the jejunum 430 cc. of the same type of substance, which was 69 per cent sediment. In the duodenum there was 150 cc. of a brown watery material which was 25 per cent sediment. The omentum and mesentery were devoid of any adipose tissue. The musculature was markedly atrophied. The mesenteric lymph glands were enlarged, and one of these exuded thick purulent

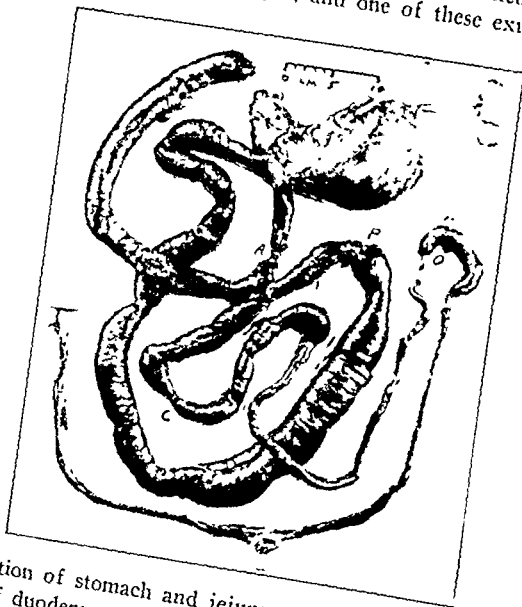


Fig. 7.—Distention of stomach and jejunum down to obstruction at *B* in dog 493. Distention of duodenum and jejunum to point of interruption at *A* and of ileum down to *C* where first intussusception occurred producing obstruction, intussusception also at *D*.

material when cut open. There was a small area of consolidation in the lungs. The other organs were grossly normal. The material from the jejunum and from the duodenum was centrifugated, decanted, filtered and passed through a Berkefeld filter. It was then sterile to culture. No demonstrable toxic effect was produced when these two solutions were injected separately into the peritoneal cavities of white mice in amounts of 0.5, 1 and 1.5 cc. The microscopic sections of the organs showed a moderate degree of central hemorrhagic necrosis of the lobules of the liver and hyperemia of the spleen. The mesenteric lymph glands demonstrated lymphoid hyperplasia. The muscle of the heart was normal. A section through the small area of consolidation showed bronchopneumonia. The kidneys were practically normal, except for an occasional tubular cast. There was some thickening in the muscularis of the obstructed jejunum, but there was

no marked change in the bowel at other points. The immediate cause of death was acute intestinal obstruction with the formation of a closed intestinal loop from intussusception in the ileum. In addition, there was beginning bronchopneumonia.

Dog 492.—First Stage: The dog weighed 14.2 Kg. A lateral anastomosis was performed in the same manner as described for dog 493.

Second Stage: The weight was 15 Kg. Twenty-six days later, a pylorectomy and anterior gastro-enterostomy were performed as described for dog 493.

Third Stage: The weight was 14 Kg. Nineteen days later an obstruction was produced, 48 cm. from the stomach; in addition, the upper part of the jejunum was sectioned as described for dog 493 (fig. 4).

There was no marked change in the behavior of the animal immediately following obstruction. The general condition was excellent even up to the twenty-eighth day, except for gradual loss of weight from 14 to 7 Kg. This was an average loss of 0.24 Kg. or 1.7 per cent per day. The dog was found dead on the morning of the twenty-ninth day. During the period of obstruction, an average

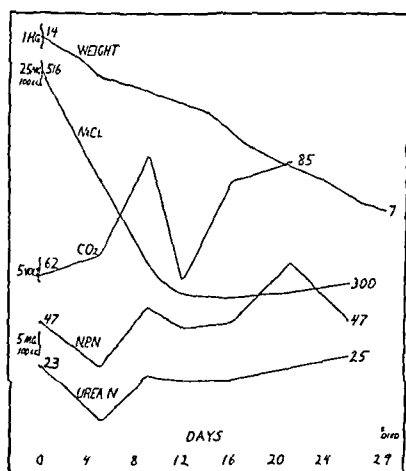


Fig. 8.—Weight and blood chemistry readings for dog 492; obstruction at 48 cm.; death on the twenty-ninth day.

amount of from 300 to 400 cc. of water was taken daily by mouth, to which sodium chloride and sometimes dextrose were added. Meat was eaten about twice a week. Vomiting occurred about every fourth day. The output of urine was from 150 to 250 cc. per day. Small stools were passed about every fifth day. The blood chlorides fell from 516 to 300. The nonprotein and urea nitrogen showed only slight fluctuation up to the twenty-sixth day, on which the last determination was made. There was a rise in carbon dioxide capacity from 62 to 85 (fig. 8). Autopsy revealed only moderate distention of the stomach and obstructed jejunum, which was most pronounced at the distal end, where the diameter was 2.1 cm. The bowel below this was only slightly collapsed (fig. 9). The gallbladder was gray and thickened, and contained golden yellow semisolid material. The mesenteric lymph glands were somewhat enlarged, but were not suppurative. There was pronounced muscular atrophy. The liver, kidneys, spleen, lungs and heart showed no marked gross changes. The microscopic sections revealed central hemorrhagic necrosis of the lobules of the liver which was less marked than in

dog 493. The spleen was slightly hyperplastic. The mesenteric lymph glands demonstrated slight hyperplasia. In the wall of the gallbladder there was diffuse leukocytic infiltration and hyperplasia of the lymphoid elements of the submucosa, compatible with chronic cholecystitis. The pancreas, heart muscle and kidneys were normal. There was a slight amount of hemorrhagic exudate in the alveoli of the lungs. Death was due to the long-standing obstruction and starvation. There is a possibility that chronic cholecystitis was a factor.

Dog 489.—The three stages as described for dog 493 were performed at intervals of three weeks. The weight at the time of the first was 21 Kg., for the second 24.4 Kg. and for the third 21.4 Kg. The obstruction was produced 76 cm.

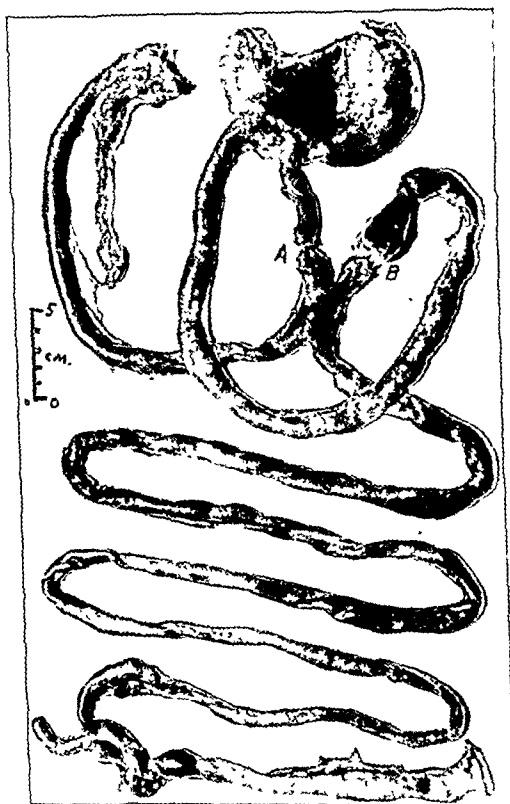


Fig. 9.—Slight distention of stomach and jejunum down to obstruction at *B*, in dog 492. Duodenum and jejunum, interrupted at *B*, emptying into ileum through lateral anastomosis.

from the stomach. The general behavior of the dog was practically normal following the obstruction, its general condition remaining good until after the twenty-ninth day. It then became weak and could not stand or even sit up. It died on the afternoon of the thirty-third day. About 500 cc. of water was taken by mouth daily, to which 1 Gm. of sodium chloride was added every second or third day, and occasionally dextrose or milk. On the average of every third day a small feeding of meat was given, which was eaten with considerable relish. About 300 cc. of urine was voided daily; a trace of albumin was observed during

the last week on two examinations. Vomiting occurred on the average of every third day. Just before death, a liter of thick gray fluid was vomited. Small stools were passed about one or two times a week. The weight declined from 21.4 to 10.9 Kg., practically half of the original weight; the average loss was 0.32 Kg. or 1.48 per cent per day. The blood chemistry showed a fall in chlorides from 528 to 236. The carbon dioxide capacity, after a preliminary drop during the first ten days, rose from 62 to 127. The nonprotein nitrogen, after a similar preliminary fall during the first week and a half, rose with some fluctuation during the third and fourth week and was high on the last day of life; the total change was from 43 to 320. The urea nitrogen paralleled the nonprotein nitrogen and changed from 21 to 104 (fig. 10). Autopsy revealed distention of the stomach and obstructed jejunum, which was most marked in the distal 9 cm. where it measured 4.5 cm. in diameter. The duodenum was moderately distended, mea-

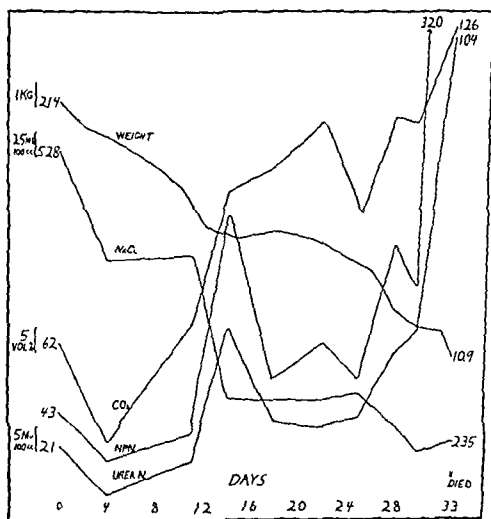


Fig. 10.—Weight and blood chemistry readings for dog 489; obstruction at 75 cm.; death on the thirty-third day.

suring 2 cm. in diameter. The bowel below the entero-anastomosis was collapsed. The stoma of this anastomosis was almost closed, barely admitting the tip of a hemostat. This stenosis had apparently caused a partial obstruction and dilatation of the duodenum (fig. 11). The lungs, heart, kidneys, liver, spleen and pancreas showed no gross changes. Muscular atrophy was marked, and there was practically complete absence of adipose tissue. The mesenteric lymph glands were enlarged and soft but not suppurative. The stoma of the gastro-enterostomy admitted three fingers. There was a small ulcer, about 0.8 cm. in diameter, at the junction of the gastric and jejunal mucosa at the distal end of the stoma. The stomach and jejunum contained thick gray material; the duodenum contained watery brown fluid. The microscopic sections also showed hemorrhagic necrosis in the central portion of the lobules of the liver. The kidneys were apparently normal except for occasional evidence of tubular degeneration. The lungs revealed some hypostatic congestion with recent hemorrhagic exudate. The section of the spleen showed a large number of phagocytic pigment-containing cells. There was

hyperplasia in the section of the lymph gland. The pancreas, gallbladder and muscle of the heart were normal. The obstructed jejunal wall showed some thickening in the muscularis. In the section through the gastrojejunal ulcer, the normal gastric mucosa was present up to the margin of the ulcer where there was a defect, the floor of which was made up of granulation tissue. Normal jejunal mucosa was present on the other side of the defect. Sections of the rest of the bowel were normal. Death was due to the long-standing obstruction and starvation without any evidence of complication other than a small gastrojejunal ulcer which probably did not hasten the time of death.

TECHNIC

Morphine-ether anesthesia and aseptic technic were used throughout. The end-to-side and lateral anastomoses were made with two rows of sutures. The



Fig. 11.—Marked distention of stomach and jejunum down to obstruction at *B* in dog 489; moderate distention of duodenum and jejunum down to *A*, where it was interrupted; collapse of bowel below obstruction and the lateral anastomosis.

bowel was interrupted by clamping, doubly ligating, cutting between the ligatures and then invaginating the stumps with purse-string sutures. In the last four dogs, side-to-side anastomoses were used entirely; the results were better, as there was less danger from leaks. Whenever the bowel was interrupted in these last four dogs, the invaginated ends were approximated by tying the two purse-string sutures together. This not only prevented intussusception of the distal part of the bowel, which otherwise occurred frequently, but also diminished the chance for the proximal part to blow out when the bowel became distended. Because of the high operative mortality in the two-stage procedure, the three-stage was adopted. This gave far better results. In a small series in which the obstruction and the anastomoses were performed at one time, the mortality rate was 100 per cent. There was a marked tendency to loss of weight following the preliminary operations, and it was often impossible to overcome it even by forced feeding with hamburger and milk. This was especially true if the

secretions emptied into the lower ileum; and was even more likely if the secretions did not have an opportunity to flow through the upper segment of jejunum as in the first three dogs. The factor which appeared to influence the results most favorably was the bringing of the weight up to normal or better before proceeding with the next stage. Dog 337 was the only one of a series of eight that survived the first stage. In a series of eighteen animals operated on like dog 515, eight survived the first stage and when obstruction was performed, six died before the sixth day from a complication; however, one lived for thirteen days with a low obstruction near the cecum. In two dogs of the series of five which survived the second stage as described for dog 983, chronic jejunal ulcer developed. In one it occurred opposite the stoma, which perforated and caused general peritonitis and death. In the other animal, three ulcers were found in the jejunum just beyond the gastro-enterostomy. The best results were obtained by the three-stage procedure as described for dogs 493, 492 and 489, these representing a third of the dogs used in this series. Concerning the blood chemistry, the plasma carbon dioxide capacity or combining power was determined in volumes per hundred cubic centimeters by the van Slyke method. The total whole blood chlorides were estimated as sodium chloride by Whitehorn's modification of Volhard's technic. The nonprotein and urea nitrogen determinations were made by Koch and McMeekin's method.

COMMENT

Although the average length of life of dogs in which high intestinal obstruction has been produced is from two to eight days, according to Haden and Orr,⁸ it has been prolonged by several methods. The short-circuiting procedure described in this paper has resulted in prolonging it more than a month. Eisberg and Draper,⁹ in a brief report of short-circuiting operations similar to that described for dog 337, stated that animals lived as long as seventeen days. When from 1 to 2 per cent sodium chloride solution is injected subcutaneously or intravenously daily into dogs with simple high obstruction, they live from three to four weeks.¹⁰ Similarly, two dogs into which sodium chloride solution was injected in the same manner for the first five days, followed by a period of starvation, lived for twenty-one and twenty-eight days, respectively.¹¹ If the pancreatic ducts are ligated¹² and obstruction is then produced, dogs will live somewhat longer than the average, but life is not strikingly prolonged.

There is no clear explanation for the increased length of life of dogs with the biliary, pancreatic and duodenal secretions short-circuited

9. Eisberg and Draper: Intestinal Obstruction, *J. A. M. A.* **71**:1634 (Nov. 16) 1918.

10. Haden and Orr (footnote 8). Hartwell; Hoguet, and Bickman: An Experimental Study of Intestinal Obstruction, *Arch. Int. Med.* **13**:70 (May) 1914.

11. Foster, W. C., and Hausler, R. W.: Acute Intestinal Obstruction: Simple Obstruction, *Arch. Int. Med.* **36**:31 (July) 1925.

12. Sweet; Peet, and Hendrix: *Ann. Surg.* **63**:720, 1916. Eisberg: *Ann. Surg.* **74**:584, 1921.

below the point of obstruction of the bowel. If it is assumed that the cause of death in obstruction is a toxin, it would seem that these three secretions or one or a combination of any two must be responsible for the elaboration of the toxin in the obstructed bowel, because short-circuiting them below the obstruction prevents the rapid occurrence of death that ordinarily ensues. It is difficult to decide which of the secretions might be responsible for the formation of toxin. The bile has been separately excluded from the obstructed portion of the bowel without any appreciable effect on the length of life by Eisberg,¹³ Draper¹⁴ and others. The pancreatic secretion has been considered by Eisberg,¹³ Sweet,¹⁵ Draper and Maury,¹⁶ Sweet, Peet and Hendrix¹² and others as the important factor in the formation of the toxin. The duodenal secretion has been held to be the source of the toxic agent by Whipple, Stone, and Bernheim,¹ Bunting and Jones,¹⁷ and others.

Aside from the theory of the formation of toxin in the obstructed bowel another factor that must be considered is the loss of digestive secretions. In dogs approximately 500 or 600 cc. of bile, a like amount of pancreatic juice and about 100 cc. of duodenal secretion are poured into the upper end of the jejunum daily. When this amount of fluid empties into a short, obstructed loop of jejunum, it could hardly be expected to be absorbed daily. Its loss through vomiting without replacement would certainly produce a serious disturbance in the water balance of the body. These secretions are rich in minerals, and the loss of this amount of mineral matter without replacement would also be injurious to the mineral balance of the body, especially because of the loss of sodium and of chloride ions.⁶ Although a biliary fistula or a duodenal fistula from which the bile and pancreatic juice have been excluded are compatible with life, a pancreatic fistula causes death in a few days.¹⁸ In this experiment, in which all three secretions empty into the bowel below the obstruction, the prolongation of life for a month or more might well be explained on the basis of the prevention of a marked disturbance of the water and mineral balance of the body by resorption of these three secretions in the lower bowel. However, a point against this being an important factor is that death occurs in two or three days in pyloric obstruction despite the fact that the secretions poured into the duodenum are below the point of obstruction. In this case the gastric secretion is lost. In the

13. Eisberg (footnote 12, second reference).

14. Draper: *Am. J. M. Sc.* **137**:725, 1909.

15. Sweet: *Penn. M. J.* **16**:520, 1912-1913.

16. Draper, J. W., and Maury: *Death in Acute Intestinal Obstruction and Kindred Conditions Due to Physiologic Disturbance*, *J. A. M. A.* **54**:5 (Jan. 1) 1910.

17. Bunting and Jones: *J. Exper. Med.* **17**:192, 1913.

18. Elman and McCaughan: *J. Exper. Med.* **45**:561, 1927.

experiment with the three secretions short-circuited below the high obstruction, there is a short segment of jejunum connected with the stomach from which there might be absorption of gastric secretion to some extent or in which changes might take place which alter the picture from that produced by pyloric obstruction.

The clinical application of the results of this experiment depends on the interpretation which is made. If it is assumed that a toxin is formed in the obstructed portion of the bowel, this would favor the use of jejunostomy at the time that an acute obstruction is relieved surgically to aid in the elimination of the stagnated toxic material as well as to lessen the distention believed to influence the absorption of the toxin. On the other hand, if it is assumed that death is due to a failure of resorption of the three normal digestive secretions, a jejunostomy at the time of operation for obstruction would be contraindicated, because it would drain off material which would be of more value to the body if resorbed. An exception to this would be when the distention of the obstructed bowel was of such a degree that there was danger of perforation unless a jejunostomy was performed. Instead, the administration of large amounts of 0.9 per cent of sodium chloride solution subcutaneously or intravenously would be indicated to replace immediately the water and minerals which had been lost by failure of resorption.

SUMMARY AND CONCLUSIONS

1. When ¹⁹ high obstruction was produced in six dogs, in which the biliary, pancreatic and duodenal secretions had been short-circuited into the bowel below the point of obstruction, they lived from twelve to thirty-three days.

2. The general behavior of these dogs was not markedly changed following the obstruction until a few days before death. They drank from 300 to 500 cc. of water a day, ate meat occasionally, vomited about twice a week, averaged an output of from 200 to 300 cc. of urine a day, and passed small black or brown stools about twice a week.

3. The weight of these dogs gradually declined as much as one-half in those which lived the longest; the average loss was 0.3 Kg. or 1.73 per cent per day.

4. The blood chemistry showed a gradual fall in chlorides and a gradual rise in the plasma carbon dioxide capacity. The nonprotein and urea nitrogen often showed a slight preliminary fall during the first ten or twelve days, followed by a gradual rise, which became marked just before death.

5. Autopsy revealed distention of the stomach and the obstructed portion of the jejunum, which was most noticeable just above the point

19. Jenkins: Proc. Soc. Exper. Biol. & Med. 26:464, 1929.

of obstruction. The microscopic sections of the organs did not demonstrate any marked changes, with the exception of the liver in which there was central hemorrhagic necrosis of the lobules. Death was due to complications in most of the dogs, although the two which lived the longest died from no determinable cause other than the long-standing obstruction and starvation.

6. The explanation for this marked prolongation of life when these three secretions are short-circuited is not clear. Either these secretions are responsible for the formation of a toxin in the obstructed bowel which was prevented in this experiment, or, when resorbed in the lower bowel, they prolong life by preventing a marked upset in the water and mineral balance of the body, which is thought to be the case when they fail to be resorbed.

LOCALIZATION OF BACTERIA IN TISSUES OF LOWERED RESISTANCE *

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The secondary infection of a so-called sterile abscess, by the intravenous injection of streptococci, is an outgrowth of work on post-operative wound infection in which we are engaged. We are attempting to arrive at a method by which the incidence of such infections can be reduced. As part of this work we induced infection with a known number of bacteria in a surgical wound in a dog, and then irrigated the wound with various antiseptic and germicidal solutions. We observed that an ordinary wound would heal, after contamination with a certain number of bacteria, without gross evidence of infection, such as oozing of pus, pus pockets, prolonged induration or sloughing of tissue. We also noted that certain wounds copiously irrigated with antiseptic solutions, would become infected even though the number of bacteria in each wound was less than that which a wound would usually dispose of without becoming grossly infected. In view of these facts we felt that another factor was involved; namely, that the traumatized or injured tissue of surgical wounds, because of its lowered resistance, might attract micro-organisms that were circulating in the blood.

Hematogenous infection of wounds is recognized clinically, yet scientific proof of its occurrence is infrequent. Findlay,¹ however, gives an excellent résumé of publications referring to this subject. He believes that histamine-like substances liberated in the traumatized places are the specific agents which cause organisms present in the blood stream to localize in these places.

Frank,² in reporting rare complications following scarlet fever, mentioned two children, aged 5 and 6 years, respectively, each of whom received 25 cc. of scarlet fever immune serum in the gluteal muscles on the second day of the disease. The temperature dropped to normal by the next day. In each case, on the fourth day of the illness, the

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* From the Division of Experimental Bacteriology, The Mayo Foundation.

1. Findlay, G. Marshall: *Histamine and Infection*, J. Path. & Bact. **31**:633, 1928.

2. Frank, Heinz: *Klinische und bakteriologische Beobachtungen an einigen seltenen Scharlachkomplikationen*, Deutsches Arch. f. klin. Med. **160**:159, 1928.

temperature rose again, and there was tenderness at the site of the injection of the serum. Four days later, at the site of these injections there developed an abscess from which hemolytic streptococci were isolated in pure culture. The author concluded that either the streptococci were present in the tissues before the injection of the serum or they entered afterward.

Since surgical asepsis is only relative, we felt that the easiest and surest way to obtain traumatized, yet sterile, tissue was through the production of a sterile abscess. We tried various methods. Boiling water sometimes produced an abscess, yet the results were not uniform. Different strengths of aqueous solution of silver nitrate were tried. Weak solutions produced only superficial necrosis of the skin. A 10 per cent solution, however, caused localized edema, with resultant necrosis of the overlying and underlying tissues, and the picture was fairly constant. Definite caseation and purulent secretion did not result in these places, yet a serous fluid could be aspirated from them for culture. It was essential that silver nitrate should not get into the peritoneal cavity, for every rabbit in which this inadvertently happened died. Consequently, we did not attempt intramuscular injection, but made all injections subcutaneously.

METHOD

Rabbits were used exclusively, and the following procedure was adopted: After the hair had been removed from the abdomen and lower part of the chest of a rabbit, blood was aspirated from the heart, and cultures made from it were sterile. Two abscesses were then made on the abdomen by a subcutaneous injection of from 1.5 to 2 cc. of a 10 per cent aqueous solution of silver nitrate for each abscess. Six to ten hours later, except in the control rabbits, green-producing streptococci were injected intravenously. The strains of bacteria used were three strains of green-producing streptococci. Each of these strains had been obtained from the gallbladder of rabbits which had been given intravenous injections of streptococci that had been obtained on culture from surgically resected gallbladders in clinical cases. We used such strains because they are not the common contaminants in work with rabbits, and especially because they had shown elective localizing power which, if inherent long enough, might be used later for identification purposes. The dosage employed varied from 5 to 7 cc. and was that usually employed in animal tests.

RESULTS

Usually, within twenty-four hours after the injection, blood cultures were again sterile. Four or five days after injection, the sites where silver nitrate had been injected were raised and edematous. Fluid was aspirated from these places.

We had two sets of controls. In the first row of the table are listed six rabbits, blood cultures from which originally were sterile. Silver nitrate was then injected, and fluid, aspirated from the abscesses four or five days later, did not produce growth in culture. The five rabbits in the second row were treated similarly, and cultures made from fluid from the abscesses in all five also were sterile. After we had proved that cultures from these abscesses were sterile, we injected streptococci intravenously. Even then, the blood of these rabbits became sterile; nevertheless, we were able to isolate the streptococcus from the abscesses of two of the five rabbits. Perhaps the reason for our failure to isolate the streptococcus from the abscesses in the three other rabbits was because of the fact that the processes of healing were rather far along by the time we made the cultures. Therefore, possibly the injected bacteria were unable to penetrate the tissue to enter the

TABLE.—*Experimental Infection of Sterile Abscesses by the Intravenous Injection of Streptococci Isolated from a Gallbladder Removed at Operation*

Number of Rabbits	Bacteria Injected	Culture		Bacteria Injected	Culture		Necropsy Data		
		Blood	Abscess		Blood	Abscess	Blood	Gall- bladder	Other Organs
6	..	000 000	000 000	0000	0000	0000
5	..	000 00	000 00	5	000 00	++	000	000	000
7	7	0000 000	++++ +++	0000 000	++++	0000 000
2	*	00	++	00

* Culture of abscess.

abscesses. In the third row are listed seven rabbits which at the beginning of the experiment gave negative blood cultures. They then received injections of silver nitrate and, six to ten hours afterward, received an intravenous injection of green-producing streptococci. After four or five days, a green-producing streptococcus was recovered from the abscesses of all seven rabbits, whereas the blood cultures of all were negative. At necropsy, a green-producing streptococcus was recovered from the contents of the gallbladders of four of the seven rabbits that received injections. In two of these four rabbits there were also gross lesions of the wall of the gallbladder. In the third rabbit, the bile was pale brown-green and thin, whereas in the fourth rabbit, the gallbladder and bile were grossly unchanged. Cultures from other organs were all sterile, and there were no other gross lesions. In order to determine further whether the strain isolated from the abscess was the same as that originally injected, the streptococcus obtained from an abscess was injected into two rabbits. In the last line of the table it is shown that

at necropsy the streptococcus which had been isolated from the abscess, localized in and was recovered from the gallbladders of both rabbits when injected intravenously; all other cultures, however, were negative.

COMMENT

Since silver nitrate in a dilution of 1:1,000 is itself a germicide and prevents growth of the green-producing streptococcus in ordinary broth culture, and since we were able to isolate this streptococcus so constantly from the originally sterile abscesses but never from the control abscesses, we believe that the strains so isolated were not contaminants. Because the strains also became localized in the gallbladders of some of the rabbits and because even those strains that were recovered from abscesses tended to become localized in the gallbladder, we feel that the strain isolated from the abscess was the same strain that originally was introduced intravenously. These results suggest that bacteria tend to become localized in traumatized or injured tissues, such as may be produced easily by surgical operations. They raise the question whether a postoperative wound infection might not sometimes be of hematogenous origin in the course of transient bacteremia. They also show that bacteria may become localized in places of lowered resistance but that they also may possess selective action. In these instances, the bacteria selected the gallbladder, the region where they originally had been obtained, and this indicates that the elective localizing power of microbes, as advocated by Rosenow, is a reality.

SUMMARY AND CONCLUSIONS

1. In rabbits which originally gave negative blood cultures, abscesses made by the subcutaneous injection of silver nitrate remained sterile.
2. A number of such abscesses became infected secondarily after the intravenous injection of bacteria.
3. The organism isolated from the abscess resembled the organism originally introduced intravenously and had the same elective localizing power.
4. These results may explain why some clean surgical wounds become infected.

A REVIEW OF UROLOGIC SURGERY

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(Continued from p. 942)

BLADDER

Tumor.—Bumpus,³⁵ in a study of records of cases of tumor of the bladder observed in the Mayo Clinic, attempted to estimate the benefit which may be expected from the various forms of treatment.

If the base of the tumor cannot be seen, it is not safe to judge the operability of the growth from its size, since growths that occupy the entire cavity of the bladder frequently have pedicles not more than 1 or 2 cm. in diameter. It is the custom in the clinic to explore suprapubically in all cases of tumor of the bladder in which the general condition of the patient allows surgical treatment. Of 465 suprapubic explorations of tumors of the bladder, it was possible to institute some form of treatment in all but sixty-six. Even without treatment, suprapubic drainage afforded much relief by diminishing spasm and reducing secondary infection to a minimum.

Not until the degree of malignancy has been determined can appropriate treatment be advised. If the tumor is comparatively small and the degree of malignancy graded 1 or 2, its destruction by fulguration through the cystoscope is advisable. The chief complication in these comparatively benign growths is recurrence; Crenshaw estimated that there is recurrence in approximately one third of such cases.

Diathermy is preferable to resection because of the slight deformity which results. Resection of a growth sometimes destroys the spherical contour of the bladder; there is a tendency to hour-glass deformity,

35. Bumpus, H. C.: The Present Methods and Results of Treating Tumors of the Bladder, *J. Urol.* **21**:371, 1929.

making it difficult for the bladder to empty satisfactorily, and residual infection occurs. Successful diathermy leaves only a scar at the site of the tumor, usually broad and not cordlike as after resection.

Radium was used extensively for several years at the Mayo Clinic in the treatment of tumors of the bladder. In some cases it was applied prior to operation through the cystoscope with the idea of irradiating the tumor so that any malignant cells left in the tissue would be incapable of reproduction. This method was not successful, since the edema following irradiation made it difficult to determine the exact extent of the tumor. In forty-six cases radium was used, sometimes in conjunction with other surgical procedures. In fifteen cases the bladder was opened and radium emanation seeds were inserted into the growth, 1 cm. apart. In twelve cases which were traced the average length of life after operation was six months.

Diathermy was used in treating tumors of the bladder which were situated in such a way or were so extensive that resection or excision was not possible. If the growth was pedunculated, it was partially removed by excision and the remainder was removed by electrocoagulation. The length of convalescence has been observed to be in direct proportion to the extent of the growth. In twenty-nine cases in which diathermy has been used for the destruction of tumors in which malignancy was graded 3 or 4, sixteen of the patients are living and four are in the third year after treatment without recurrence and in good health. Of 179 patients with tumors of the bladder of the same degree of malignancy, treated by various surgical measures, fifty are living, twenty-seven more than three years. This comparison indicates that diathermy, instead of replacing strictly surgical measures, has brought cases formerly thought to be hopeless within the scope of successful treatment.

[COMPILERS' NOTE.—Initial determination of the degree of malignancy and the size and site of the tumor, cystoscopic fulguration of small tumors graded 1 and 2, resection of small tumors when resection is not attended by marked subsequent deformity, partial resection combined with diathermy, or diathermy alone, in the more extensive tumors of higher degrees of malignancy, and a strong trend away from treatment by radium would seem to epitomize the present views of this writer.

The report gives the impression that electrocoagulation finds a wide field for application in this branch of urology, which has been so disappointing. The classification of tumors of the bladder is as yet much confused and the casual reader of urologic literature is often at a loss to correlate reports from different clinics in which a large number of patients are observed. Frontz and Barringer recently presented criteria for the treatment of tumors of the bladder by radium and

resection which are possibly somewhat at variance with the principles set forth by Bumpus in his report. The grading of epithelial neoplasms, although fairly exact in the hands of Broders and his co-workers, offers a wide opportunity for error in interpretation when applied by pathologists in general, due to the personal equation in determining degrees of cellular differentiation. Nevertheless, Bumpus has shown that electrocoagulation methods, alone or combined with resection, are likely to contend strongly for precedence over radiotherapeutic procedures in the treatment of vesical neoplasms in the immediate future.]

Wilensky and Firestone³⁶ reported a case of spontaneous disappearance of a papillary carcinoma of the bladder in a man, aged 63 years. The patient had mild diabetes and tabes dorsalis. General examination revealed that the pupils were unequal and irregular and did not react to light or in accommodation. Reflexes at the knee were absent. The Wassermann reaction was positive, + + + +. Cystoscopic examination showed a papillary tumor with a broad base about 1 cm. in diameter, on the posterior wall midway between the ureteral orifices, and just above the trigone. Pathologic examination of small specimens from the growth showed papillary carcinoma. Eight days after cystoscopic examination, a suprapubic incision in the median line was made, the bladder was opened, and its interior was exposed to full view. The entire bladder could be thoroughly and completely explored and palpated. A tumor was not present; the site from which the specimen had been taken at biopsy could not be distinguished in any way from the remainder of the mucosa. The interior of the bladder was apparently normal. The bladder and abdominal wall were closed, and a suprapubic tube was left in for drainage. The patient died thirty-eight days afterward. Necropsy showed suppuration of the prevesical space and abdominal wall, with subacute cystitis and ascending pyelitis of the right kidney. The bladder did not show evidence of malignant growth.

Kretschmer and Barber³⁷ reported a case of carcinoma in a diverticulum of the bladder, a condition which they have observed rarely. They stated that a diverticulum may be the seat of changes that are in line with other pathologic changes which occur in the bladder, such as infection, stone, tumor and leukoplakia. Cases are generally not recognized until late in the course of the disease because patients delay in consulting physicians. The prognosis has been extremely bad in the past, and surgical results have been only mediocre.

36. Wilensky, A. O., and Firestone, Abraham: Spontaneous Disappearance of Papillary Carcinoma of the Bladder, *J. Urol.* **21**:611, 1929.

37. Kretschmer, H. L., and Barber, K. E.: Carcinoma in a Bladder Diverticulum: Report of a Case and a Review of the Literature, *J. Urol.* **21**:381, 1929.

Hunt³⁸ stated that it is not common to find primary malignant disease in a diverticulum without involvement of the bladder. He reported five cases in which the primary epithelioma was confined to a diverticulum; four of the patients he operated on.

A man, aged 62 years, was operated on by Judd. At operation a papillary epithelioma was found almost to fill a diverticulum and to protrude through the opening of the diverticulum into the bladder, but the diverticulum alone was affected. The mucosa of the bladder was free. The diverticulum was entirely excised. Six months later symptoms of recurrence in the bladder were manifest. The patient died a year after the operation.

In the second case, the patient, a man, aged 59 years, had a large, soft cystic mass, which filled the lower half of the abdomen. He died following cystostomy. At necropsy a large diverticulum was found emptying into the right wall of the bladder. In its contracted state the diverticulum was as large as the bladder; if one is to judge from the size of the abdominal mass and the cystographic data, the diverticulum must have been at least twice the size of the bladder previous to drainage. It was relatively thin-walled, and its walls did not contain muscle fibers. A large foramen about 2 cm. in diameter communicated between the diverticulum and the bladder. The right ureter, which was double, united at the bladder, entered the diverticulum, and a true interureteral bar extended from one ureteral orifice in the diverticulum, through the foramen of communication, to the left ureteral orifice in the bladder. The wall of the bladder was greatly hypertrophied. In the lateral wall of the diverticulum, below the right ureteral orifice, were two flat, malignant-appearing lesions, one about 2 cm. and the other about 1 cm. in diameter, which, on microscopic examination, proved to be squamous cell epithelioma.

The third case was that of a man, aged 55 years, in whom extravesical excision of a diverticulum of the right base and transvesical excision of the left diverticulum were performed. The diverticulum on the right side was densely adherent and because the right ureter emptied into the bladder at the orifice of the diverticulum, it was divided and subsequently reimplanted into the bladder. The diverticulum on the right was about 4 cm. in diameter and contained a primary malignant papilloma 2 cm. in diameter, graded 2, entirely confined within the diverticulum.

The fourth case was that of a man, aged 70 years, in whom suprapubic drainage of the diverticulum and bladder was instituted and maintained for about a month, when extravesical excision of the diver-

38. Hunt, V. C.: Malignant Disease in Diverticula of the Bladder, J. Urol. 21:1, 1929.

ticulum was carried out. The capacity of the diverticulum was about 1 liter. On removal of the diverticulum a squamous cell epithelioma 3 by 2 by 1.5 cm., graded 4, was found in its lateral wall away from the orifice of communication between the diverticulum and bladder and confined entirely to the diverticulum. Convalescence was satisfactory until the fifteenth day, when an attack of pulmonary embolism occurred, causing death twenty days after operation.

The fifth case occurred in a man, aged 55 years. The bladder was explored under sacral anesthesia and block of the abdominal wall. The wall was greatly thickened, and there was extensive trabeculation. In the left lateral wall, above the ureteral orifice, an opening about 1.5 cm. in diameter led into a diverticulum with capacity larger than that of the bladder. There were two additional diverticula of the base of the bladder with their openings just lateral to the ureteral orifices. These diverticula were of about equal size and were about 7.5 cm. in diameter. The prostate gland was slightly enlarged intravesically and a moderate degree of cystitis was present. Extravesical excision of the large diverticulum of the left lateral wall was readily accomplished. The diverticulum was 12.5 cm. in diameter. Examination disclosed a sessile tumor about 1 cm. in diameter situated well out in the lateral wall of the diverticulum. Microscopic examination revealed an epithelioma graded 3. Transvesical excision of the diverticulum of the left base of the bladder by the Geraghty method was made.

Stones in Children.—Balacesco³⁹ stated that stones in the bladder of children are common in Roumania. During a period of fifteen years he performed suprapubic cystostomy in seventy-six cases; stones from 1 mm. to 2 cm. in diameter were removed. The age varied from 15 months to 3 years in twenty-one cases; in twenty-five cases it was between 3 and 6 years, in fourteen cases between 6 and 9 years, and in sixteen cases, between 9 and 18 years. All the patients were boys except one, a girl, aged 3 years. In seventy of the seventy-six cases the cystostomy orifice was closed at operation; postoperative complications or long-standing fistula did not occur. In the remaining six cases, it was necessary to institute drainage, because the patient was in a generally precarious state as a result of ascending infection. Four of these patients died.

The main symptoms were incontinence, day and night, pain, sudden interruption in urination, and only rarely hematuria. A diagnosis was made in each instance by simple fluoroscopy. Balacesco stated that risk does not accompany primary suture of the bladder.

39. Balacesco: Soixante-seize cas de calculs vésicaux de l'enfant, *Bull. et mém. Soc. nat. de chir.* 15:322, 1929.

Paralysis.—Boyd and Bailey⁴⁰ stated that varying opinions exist among urologists as to the best method of handling retention of urine which occurs in cases of acute paralysis of the bladder. Some urologists advocate attempting to empty the bladder by massage of the prostate gland and pressure on the abdomen without catheterization. Other urologists advocate intermittent catheterization; a few advocate indwelling catheters, and a few, suprapubic drainage. Boyd and Bailey stated the belief that suprapubic cystotomy is the procedure of choice in almost all of these cases.

Usually in cases of injury to the spinal cord, complete paralysis of the detrusor urinae muscles and active contraction of the internal sphincter occur at once. Urine accumulates in the bladder, the bladder distends to an enormous size, and in forty-eight hours there is usually an overflow incontinence of urine. If conditions are favorable, this gives way in four or five weeks to automatic urination. Before this the bladder will gradually begin to discharge at irregular intervals more and more of the content, as the result of which capacity of the organ is reduced slowly. If so-called automatic urination develops, a large quantity of urine is expelled at each micturition.

Experience has shown that continuous drainage offered by suprapubic cystotomy is superior to intermittent catheterization in the treatment of patients with paralyzed bladders. Catheterization is thus avoided.

Eight cases of paralysis of the bladder were considered. In the first two cases operation was not performed. In the third case, in which paralysis was caused by infection of the spinal cord, suprapubic drainage relieved symptoms in the bladder. The fourth case was one of traumatic fracture of the spine. Drainage was established on account of severe infection. In the fifth and sixth cases the return of function was sufficient to permit removal of the suprapubic tube. In the two remaining cases the patients were paralyzed for life by traumatic accidents. Infection of the bladder developed after catheterization. The patients were in good health except for paralysis, one patient, twelve months, and the other nine months, after suprapubic drainage.

Priestley⁴¹ stated that vesical paralysis is more likely to be caused by malignant tumors in the spinal cord than by benign tumors. Tumors in the cervical region, benign or malignant, cause vesical paralysis less frequently than tumors in any other situation. Malignant tumors cause paralysis of the bladder earlier after the appearance of the first neurologic sign than do benign tumors. Symptoms in the bladder may

40. Boyd, M. L., and Bailey, M. K.: Suprapubic Cystotomy in Bladder Paralysis, *J. Urol.* **21**:623, 1929.

41. Priestley, J. T.: The Spinal Cord Bladder, *J. Urol.* **21**:635, 1929.

be expected about six months after the first symptom in the cord, but there are wide variations in this time relationship. The usual symptoms in the bladder resulting from a tumor in the spinal cord are difficulty of urination, retention and incontinence of overflow. In cases of trauma to the spinal cord, retention is present from the start.

The treatment of choice for retention due to lesions of the cord is noncatheterization and the development, if possible, of normal function of the bladder. If this fails, emptying of the bladder by suprapubic pressure is preferable to catheterization. In some cases suprapubic cystotomy is necessary. Priestley considered that the most important factors in the development of normal function of the bladder are noncatheterization, the utilization of mass reflex action, the systematic use of suprapubic pressure and the presence of a noninfected bladder.

[COMPILERS' NOTE.—Infection in a paralyzed bladder is a condition which every urologist approaches with apprehension. If there is retention, the easiest way is often chosen by the attending physician who catheterizes the patient before a urologic consultant is called. Priestley emphasized that if infection is to be avoided and the development of autonomic emptying is to be achieved, the catheter is to be held in abeyance even at the expense of cystotomy. Urologists and neurologic surgeons of the present day seem generally to concur in this opinion.]

Fistula.—Legueu⁴² used the following method of transperitoneal closure in twenty-four cases of vesicovaginal fistula, with entirely satisfactory results. The patient is placed in an extreme Trendelenburg position, the abdomen is opened, and a self-retaining retractor is inserted. The peritoneal fold, which is reflected from the posterior wall of the bladder across the vaginal vault, is then exposed and brought into view. An incision is next made in the median line through the posterior wall of the bladder and vault of the vagina so as to expose the fistulous openings. The vagina and bladder are separated by means of sharp dissection until the fistulous openings are completely isolated. The bladder is mobilized on all sides at a distance from the fistula. The openings in the bladder and vagina are closed with interrupted catgut sutures. The peritoneal edges are approximated with fine chromic catgut and the incision through the abdominal parietes are closed in the usual manner.

In the postoperative treatment of vesicovaginal fistula, overdistention of the bladder should be prevented by the introduction of a permanent catheter into the bladder or by catheterization every four hours.

42. Legueu, Felix: The Transperitoneal Closure of Vesicovaginal Fistulae, Surg. Gynec. Obst. 48:796, 1929.

[COMPILERS' NOTE.—The suprapubic approach, alone or combined with the vaginal route, for the treatment of vesicovaginal fistula seems to be growing in popularity. Young described a transvesical suprapubic operation in 1927. His closure of the fistula was accomplished entirely from the intravesical site. In the same year Roeder described a vaginal operation. He closed the fistula by dissecting free large vaginal flaps which were sutured together, the first suture line being inverted toward the bladder and this inversion being maintained by drawing the suture ends up through a cystotomy opening. Apparently Leguen attacked the fistula extravesically but from within the abdomen, which is somewhat of a departure from the usual technic.]

PROSTATE GLAND

Hypertrophy.—Randall⁴³ commented on, two different types of prostatic enlargement called "middle lobe." Anatomically there are two different glandular elements situated in the median line posteriorly, the posterior commissural glandular tissue, and the subcervical glandular tissue of Albarran. Either may undergo hypertrophy independently of the other or independently of growth of the lateral lobe. Likewise, either may undergo hypertrophy in conjunction with enlargement of the lateral lobe or in conjunction with one another. When the posterior commissural glandular tissue hypertrophies, it first causes thickening and elevation of the posterior vesical lip. On further hypertrophy the commissural tissue raises upward the apex of the trigone, the vesical lip, and the first portion of the floor of the urethra. The sphincter gradually drifts backward and behind the hypertrophying mass, and the hypertrophy is constantly confined by the prostatic capsule and always under the trigonal muscle. It ultimately grows to form a flat, thumblike projection in the cavity of the bladder, with widely separated clefts in the posterolateral angles. In cases of long standing, hypertrophy of the lateral lobes becomes evident. Hypertrophy of the subcervical gland starts as a small, rounded nodule just infrasphincteric and quickly becomes spheroidal. When it is large enough to push up through the sphincter, pedunculation has started, after which this characteristic is never lost or absent. Its only covering is the mucous membrane and its only attachment is its own ducts which form a definite pedicle.

A differential diagnosis may be made by combined rectal and cystoscopic study. On rectal examination, the posterior commissural hypertrophy presents a flattening out of the median prostatic groove with a broad flaring out of the upper lateral limits of the lobe and

43. Randall, Alexander: Genesis, Morphology, and Surgery of Prostatic Middle Lobe Hypertrophy, *Ann. Surg.* 88:112, 1928.

a greater mass of tissue in the intervacular, subtrigonal region. Cystoscopic examination reveals generalized thickening of the posterior vesical lip, partial or complete obscuring of the trigone, and, with retraction of the instrument, a long distance is covered before the posterior urethra is entered. With an instrument in the urethra and a finger in the rectum, the thickened mass is readily felt, as the instrument easily remains in the median line and rides over the hypertrophic lobe. Subcervical hypertrophy of the gland, because of its pedunculated character, presents easily recognized variations. The growth is intravesical; rectal examination is usually unsatisfactory and misleading. If the cystoscope is passed it invariably enters to one side or the other of the lobe, which may be mistaken for the rotundity of enlargement of the lateral lobe.

The enucleation, starting intra-urethrally, includes about one lateral lobe and should pass across the urethra and the apex of the trigone. Then the finger goes directly around the opposite lateral lobe, and the prostatic mass is removed in one piece. In hypertrophy of the subcervical gland, its mucous membrane should not be saved but should be pinched off at once. Randall usually placed a clamp on the lobe, simply twisting its pedicle to the point of rupture. If hypertrophy of the lateral lobe also is present, the suprapubic enucleation entails the removal of the subcervical lobe, and the encucleation of one lateral lobe, and the removal of the other lateral lobe.

In perineal prostatectomy, subcervical hypertrophy presents a peculiar complication, since it does not lie within the prostatic capsule. Because the prostatic capsule is approached on its posterior surface, a complete lateral lobe and commissural growth may be removed, and hypertrophy of the subcervical lobe may be missed entirely. If clean enucleation has been performed on the lateral lobes, a subcervical lobe should be removed as follows: the prostatic tractor is withdrawn entirely, and with a spoon retractor or lobe forceps, entered through the urethrotomy incision, the lobe is grasped and an attempt is made to draw it down through the posterior urethra to a point at which its attachment may be ruptured and the mass may be removed. Because of such difficulties with hypertrophy of the subcervical gland, Randall stated the belief that this type of enlargement belongs essentially to the suprapubic type of operation.

[COMPILERS' NOTE.—This differentiation of two types of median-lobe hypertrophy is often disregarded, especially by those who practice suprapubic operative technic and who clean out the intracapsular tissue from above. Although the subcervical gland type is not intracapsular, it will undoubtedly be removed when the intracapsular enucleation is done. In perineal prostatectomy it is possible entirely to escape the

removal of the nodular subcervical gland unless the precautions outlined by Randall are observed.]

Deaver⁴⁴ described his technic for closure of the prostatic bed in suprapubic prostatectomy. He does not use either the prostatic bag or gauze packing. The wound in the bladder is retracted laterally and fore and aft, with the use of the proper-sized Deaver retractors. A small, moist gauze pad is introduced into the fundus of the bladder, over which the upper retractor is placed, so that when traction is made the floor of the bladder will be level. This gives a good view of the wall of the bladder, the prostate gland, the ureteral orifices, and, after removal of the prostate gland, the prostatic bed. The margins of the wound are grasped and retracted with Allis forceps. An assistant places a finger in the rectum and carries the floor of the prostatic bed upward into the opening of the bed. With the aid of a Cameron light, bleeding points are ligated, and, with a curved needle of proper size and shape, the walls of the bed are approximated laterally up to the torn end of the urethra. A soft rubber catheter is then carried into the bladder through the urethra and left in; a large rubber tube is placed in the bladder and the wound is closed up to this tube. A small piece of rubber-dam is placed in the prevesical space and removed on the second day. The suprapubic tube is taken out as soon as the urine is clear, and the catheter is left in the bladder until the suprapubic wound has closed, after an average of from ten to fifteen days.

Deaver expressed the belief that this technic minimizes the possibility of bleeding and infection. He does not advise closure of the prostatic bed in a badly infected bladder. He does not believe that closure of the prostatic bed is so easily accomplished in the two-stage operation on account of the more limited space and the lessened flexibility of the tissues following the primary operation.

Deaver applies his method to the large prostatic bed, which shows little tendency to contract or to ooze in spite of irrigation and hot water. With the floor of the bed and the anterior wall of the rectum carried upward by the finger of the assistant in the rectum, chromic catgut sutures may be readily inserted. There is no danger of injuring the wall of the rectum, the assistant's finger and the fascial and muscular covering of the bowel being enough in evidence to allow avoidance of accidents if the needle is manipulated gently. Deaver stated the belief that his technic is less likely to be followed by contraction and stricture than the bag or gauze pack method.

[COMPILERS' NOTE.—One of the advantages of this method would seem to be the almost immediate epithelization of the prostatic bed, a good principle in all urethral surgery. If such epithelization can

44. Deaver, J. B.: Closure of the Prostatic Bed in Suprapubic Prostatectomy, *Ann. Surg.* 88:118, 1928.

be maintained from the beginning, better healing will unquestionably ensue. Difficulties may be encountered in certain types of cases in which the prostatic enucleation has been accompanied by considerable trauma to the mucosa, which would lead to trouble in accurate approximation of the end of the urethra to the mucous membrane of the orifice of the bladder.]

Fullerton⁴⁵ stated that prostatectomy has been made less a formidable operation as a result of suitable preoperative preparation and the methods employed to control hemorrhage. The problem of infection due to inadequate drainage has not yet been solved satisfactorily. Drainage by the suprapubic route is not altogether satisfactory.

Fullerton now institutes drainage in cases of suprapubic prostatectomy through the perineum after removal of the prostate gland. The operation is carried out as follows: An incision is made in the perineum on one side, parallel to the ischiopubic ramus, and then crosses a transverse line from the bulb to the anterior part of the tuberosity of the ischium. The incision involves the skin only. The index finger of one hand is then introduced; the base of the triangular ligament is felt and the finger is passed forward to the prostate gland. In doing so it passes above the levator ani muscle. A plug of gauze is temporarily packed into the wound and the patient is placed in position for suprapubic prostatectomy, which is carried out in the usual way. With one index finger in the prostatic cavity and the other in the perineal wound, the thickness of the septum to be traversed by the forceps is estimated. The septum in some cases is almost as thin as a sheet of note paper. It is readily perforated by a long forceps, and a drainage tube about 1.25 cm. in diameter is drawn through. As it is essential to drain both the prostatic cavity and the bladder, the tube is passed well into the bladder; it is perforated by large holes up to the point at which it leaves the prostatic cavity for the ischiorectal fossa. A suprapubic drainage tube is also left in place. The perineal tube should then be left in place until the suprapubic wound has healed, and it should be clamped from time to time to encourage normal urination. The perineal wound does not leak, and on removal of the tube it heals without incident. Fullerton has not observed any infection of the ischiorectal fossa or any leakage through the perineal wound either during the time the tube was in position or after its removal. As soon as normal urination is established, the tube is removed.

Young⁴⁶ stated that he has watched Fullerton carry out his method of draining the bladder and prostatic cavity through the perineum in two cases. The procedure is done rapidly and adds little to the dura-

45. Fullerton, Andrew: Drainage of the Bladder Through the Perineum After Suprapubic Prostatectomy, *Brit. J. Urol.* 1:7, 1929.

46. Young, H. H.: Discussion, *Brit. J. Urol.* 1:15, 1929.

tion or the complexity of the operation of suprapubic prostatectomy. Excellent drainage is obtained of the prostatic cavity from which the hypertrophied lobes have been removed, and also from the bladder, without any possibility of injury to the urethral sphincter or important vessels or nerves in this region. He stated the belief that this method affords an excellent opportunity for dependent perirenal drainage of the bladder and prostatic cavity, the absence of which has been one of the chief objections to suprapubic prostatectomy. From the ease with which the prostate gland is reached by this operation, Young suggested that abscess of the prostate gland and perhaps other conditions might be dealt with by this route.

Carcinoma.—Barringer,⁴⁷ in order to illustrate the futility of treatment in most cases of carcinoma of the prostate gland, classified 202 consecutive cases with reference to the duration of life after examination and treatment. Eighteen of the 202 cases were not traced to termination. Fifteen patients lived more than three years, six lived more than four years, six lived more than five years and three lived more than seven years. Only thirty patients (15 per cent) lived for a reasonable length of time after the first examination. Only a moderately small number of those with extensive disease were benefited by treatment.

In any attempt to control carcinoma of the prostate gland, Barringer considered it essential that every man aged 55 or more should be examined by rectum with the same regularity with which blood pressure, heart and urine are examined. Ewing stated the belief that the retention of irritating secretions and inflammatory changes play some part in carcinoma of both the prostatic gland and the breast.

Certain prostatic carcinomas (approximately 5 per cent) are greatly affected by irradiation by means of either radium or the roentgen ray. If the patient is in excellent condition and has not lost weight, he should have one course of deep roentgen treatment to determine whether the carcinoma is radiosensitive. Barringer gathered evidence, from both pathologic specimens and clinical data, to show that operation rarely removes all of the prostatic carcinoma. Operation should be followed by persistent irradiation of the prostatic bed and the lymphatics around the seminal vesicles.

Fifteen of a series of twenty patients with papillary carcinoma of the bladder were free from carcinoma during the period of observation; eleven had been observed for more than five years. Of fifty-one patients with infiltrating carcinoma of the bladder, eighteen were free from the disease; twelve had been free for more than five years.

47. Barringer, B. S.: *Carcinoma of the Prostate and Bladder*, New England J. Med. 198:117, 1928.

Previous to 1927, Barringer made ninety-four suprapubic implantations of radium in ninety cases, with a mortality of slightly more than 3 per cent. Operation was performed in two cases; both patients died. One patient, who was operated on three times, was alive and free from carcinoma seven years after the first operation. There were five cases of papilloma, ten of papillary carcinoma and seventy-nine of infiltrating carcinoma. The mortality after radium compared with the mortality after operative removal of carcinoma of the bladder (between 10 and 20 per cent) shows that by the use of radium a good number of lives might be saved.

Barringer pointed out several significant factors in the performance of the suprapubic implantation of radium: (1) the contents of the bladder should not be spilled into the open wound; this is best prevented by emptying the bladder by means of an aspirating device, padding the wound well, and removing any soiled pads after the bladder is empty; (2) removal by cautery of the quickly heating electric type of protruding parts of the tumor to minimize bleeding and control infection; this method is particularly valuable if the tumor is of the sloughing, badly infected type; (3) if the tumor is large and if bleeding has been severe, or if the bladder is badly infected, drainage should be instituted; a rubber drainage tube should be inserted and removed when bleeding has stopped or when infection has been controlled, generally at the end of several days, and (4) the radium method of choice is the implantation of gold tubes of radium, of a strength of about 2 cm., placed 1.5 cm. apart throughout the base of the growth.

[COMPILERS' NOTE.—Barringer's statistics are noteworthy, confirming as they do the rather ominous outlook for cure in carcinoma of the prostate gland, regardless of the type of treatment employed. The report of Bumpus (1926) from the Mayo Clinic revealed clearly how futile efforts in this direction have been. At that institution, surgical or radiotherapeutic procedures are not usually employed except in cases in which there is definite obstruction or in which the condition is discovered in the course of prostatectomy for lesions which are clinically benign.

However, Barringer and Young have not been so pessimistic and stated the belief that, although cure from radium or prolongation of life may seldom be effected, yet its application, together with deep roentgen treatment, may frequently make the patient more comfortable. Young has also reported a few cases of cure over a period of years from his radical operation. Practically, it would seem from the statistics available that there is little to offer the patient with prostatic carcinoma except in early cases in which carcinoma is found in hypertrophied prostate glands after surgical removal. Here intensive roentgen or radium treatment or a combination of both is said to give fair results.

Barringer has long been an advocate of the method of implanting radium seed in papillary carcinoma of the bladder. Even yet the clinicopathologic classification of neoplasm of the bladder is confused, although the work of Broders in grading these tumors seems to be gaining acceptance and is doing much to stabilize ideas on the subject. Thus Bumpus, in a recent article, designated epitheliomas graded 1 or 2 (Broders' classification) as amenable to successful treatment by endoscopic fulguration, cauterization or electrocoagulation by diathermy through a cystotomy opening when the growth is extensive. Tumors graded 3 and 4 are to be treated by resection or by diathermy applied through the open bladder when the extent and site of the growth makes resection impossible. The patient is enjoined to report for cystoscopic examination every few months; at such times recurrences are diligently sought and, if found, fulgurated. Thus urologists at the Mayo Clinic write in a hopeful spirit, and their initial results seem to justify the method. Nevertheless there are those who follow Barringer and believe that implantation of radium seed still has a distinct field of usefulness.]

Wildbolz⁴⁸ stated that operative procedures in cases of prostatic hypertrophy are successful and satisfactory. The operation is still a formidable procedure and has not been attended with good results. In the last twenty years a few cures have been reported. Because of the poor results generally obtained from operation, attention was directed to roentgen and radium treatment. Little benefit seemed to be derived from either, and in some instances the growths appeared to be stimulated. In recent years many surgeons have resorted to palliative measures, such as catheterization and suprapubic drainage.

Only in recent years have statistics of operation for prostatic carcinoma become available. Bumpus reported 164 cases, in twenty-one of which the patients were living and well five years after operation. Even if patients were not cured, life was prolonged. Young reported on twenty of his own patients, fourteen of whom (70 per cent) were living and well three years after operation. Marion reported that the majority of patients on whom prostatectomy had been performed for carcinoma was alive and free from urinary distress from one to five years after operation. Two of the patients were alive four and six years after operation, although local recurrence could be demonstrated. Only three of the forty-eight patients appeared to be cured ten, seven and four and a half years after operation. Wildbolz operated on forty patients with carcinoma of the prostate gland. Three of these (7.5 per cent) died after operation of other complications; two were not traced. Thirteen (30.2 per cent) died from one and a half to

48. Wildbolz, Hans: Die Erfolge operativer Therapie des Prostatakarzinoms, Schweiz. med. Wchnschr. 58:726, 1928.

three years after operation from multiple metastasis or local recurrence; four died from one to three years after operation from intercurrent disease without signs of recurrence. In six cases there was no sign of recurrence from one to three years after operation. Twelve patients (30 per cent) lived longer than three years without any sign of recurrence, but two of them died of recurrences six and nine years after operation; they had been regularly examined and had not shown signs of carcinoma until the stated time. A third patient died fifteen years after operation, at the age of 85 years, from severe cystitis, but without evidence of prostatic enlargement. Wildbolz had observed the condition of this patient for ten years without noting signs of recurrence. Of the remaining patients who lived longer than three years and were free from recurrence, one lived nine years after operation, two lived six years, and one patient lived five years. Five patients are still living fourteen, ten, six and four (two patients) years after operation.

The condition was operable in only forty of the 145 patients; 105 were treated symptomatically and died in from one to three years. Wildbolz stated the belief that early diagnosis is one of the prime factors in any attempt to cure carcinoma of the prostate gland by surgical measures. Symptoms of prostatic carcinoma are not apparent until late in the course of the disease. According to the literature, in from 15 to 20 per cent of the cases of prostatic enlargement the condition is malignant. Wildbolz noted that one of every five to six patients with prostatic enlargement had carcinoma. Bleeding from the gland has been found to occur only rarely in carcinoma; it usually occurs in benign hypertrophy of the prostate gland. Neurologic pains in the region of the perineum, sacrum or thighs are usually indicative of the extension of the tumor outside the prostatic capsule.

Rectal palpation of the prostate gland is the only method of determining carcinoma early. As soon as one or both lobes lose their resilience and become boardlike or nodular, carcinoma is definitely indicated. Inflammatory induration and prostatic calculi should be differentiated. Stones are to be differentiated by a crunching sensation on palpation. Most inflammatory tissue is not so hard as carcinomatous tissue, although there are difficult borderline cases. Wildbolz erred in the diagnosis in two cases. Carcinoma of the prostate gland is not always to be felt rectally. The soft type of malignant growth is rare. Young found seven cases in 250 cases of prostatectomy. Wildbolz found three cases in his series.

Wildbolz agreed with Young that the perineal route is superior to the suprapubic for prostatectomy, since there is always a possibility that carcinoma will be found. By this route the prostatic capsule and seminal vesicles may be removed if necessary. By cutting through the

prostatic capsule, carcinoma may be identified even before enucleation is begun; thus it is possible to change the operative technic. Even with complete resection of the prostate gland and capsule, the sphincters may be seen and saved, and continence will be as satisfactory as after the suprapubic operation. Wildbolz stated that the objections, prolonged healing of the wound, the formation of fistula, and incontinence, have not been encountered in his cases in which operation has been performed by the perineal route.

[COMPILERS' NOTE.—It is unfortunate that there is no criterion for the early diagnosis of malignant conditions of the prostate gland. If such a diagnosis can be made by palpation rectally or by biopsy by the urethra, frequently the process is too far advanced for surgical procedures to offer anything more than palliation. Methods of obtaining tissue by perineal incision are mainly unsatisfactory. Also, the symptoms are often obscure and the patient and the family physician confuse the condition with arthritis, sciatica and neuritis until the disease is advanced. Bumpus, in a review of a large number of cases, stated his belief that the best chance for cure is in the early cases in which histologic diagnosis has been made from the gland that has been removed presumably for benign disease. Since the incidence of carcinoma in disease of the prostate gland is one in five or six, and the suprapubic operation is totally inadequate for the treatment of malignant disease, we agree with Wildbolz that this is one of the strongest arguments for the perineal operation in prostatic hypertrophy.]

Abscess.—Peterson⁴⁹ stated that abscess of the prostate gland may occur by direct extension of a gonorrheal infection in the posterior part of the urethra, or by metastatic involvement of the gland and from some distant or general infection.

Peterson reported seven cases of abscess of the prostate gland. In operating he introduces the Young prostatic tractor into the bladder in order to pull the prostate gland against the perineum. He uses the inverted U-incision, the skin and fat being cut through. Blunt dissection is then carried out on each side of the central tendon of the perineum, with exposure of the prostatic capsule. The central tendon is not severed but is pulled to one side of the median line by narrow-bladed retractors. A longitudinal incision is made into the gland and the cavity is explored with the finger to break down any septums.

Peterson noted that softening and fluctuation of the prostate gland is not a constant observation in the presence of an abscess. In some cases he was not certain that abscess existed until the capsule itself had been incised and blunt forceps had been introduced into the substance of the gland.

49. Peterson, Anders: Prostatic Abscess, J. A. M. A. 92:130 (Jan. 12) 1929.

Cumming⁵⁰ reported a case of sudden massive destruction of the prostate gland, with resulting dysfunction of the bladder. Retention, incontinence and severe secondary hemorrhage were complications. A complete history, cysto-urethroscopic studies and urography are significant factors in making the diagnosis. Satisfactory surgical intervention consisted of merging of the bladder and the extravescical pseudodiverticular cavity.

URETHRA

Tumor.—Fukai⁵¹ reported four cases of carcinoma of the urethra in men; two patients died following operation. Primary carcinoma of the male urethra is relatively rare; only eighty-four cases were noted in the literature, including those reported by Fukai. In fifty-five cases (60 per cent) there was a history of gonorrhea and in 12.7 per cent a history of trauma. It was often found that the carcinoma had developed on a gonorrheal or traumatic stricture. The seat of the disease was most commonly in the pars cavernosa, with predilection for the bulb or the structures in its vicinity. The early symptoms are similar to those occurring in ordinary stricture. Fukai stated the belief that every stricture and subsequent condition should be investigated for carcinoma, especially if the stricture has occurred in old age without a history of gonorrhea or if it becomes rapidly worse. Gumma should be eliminated in the diagnosis; although of infrequent occurrence, it can easily be confused with carcinoma. Early operation is desirable.

In sixty-two cases there were thirty-four radical operations, with sixteen deaths; in the remaining twenty-eight cases the mortality was 71 per cent. Histologically, the condition in all cases is squamous cell carcinoma. The determination of glandular metastatic carcinoma can be made only histologically.

Huggins and Curtis⁵² reported a case of carcinoma of the urethra of a man in which they observed the indolent course of the lesion. Carcinoma of the urethra may cause periurethral abscess and stricture, which clinically are not distinguishable from the usual variety of primary types. If biopsy is to be effective in the diagnosis, it must include the urethral mucosa. The results from radical operation were apparently good.

50. Cumming, R. E.: Bladder Dysfunction Following Prostatic Abscess, *J. A. M. A.* **92**:128 (Jan. 12) 1929.

51. Fukai, A.: Ueber das primäre Carcinom der männlichen Urethra, *Acta derm.-venereol.* **11**:1, 1928.

52. Huggins, C. B., and Curtis, G. M.: Carcinoma of the Male Urethra with a Technique of Penis Extirpation, *Surg. Gynec. Obst.* **48**:544, 1929.

Obstruction.—Young and McKay⁵³ stated that congenital obstruction of the prostatic urethra always occurs as one of three types. In the most common type there is a ridge lying on the floor of the urethra, continuous with the verumontanum, which takes an anterior course and divides into two forklike processes in the region of the bulbomembranous juncture. These processes continue as thin membranous sheets, directing upward and forward, which may be attached to the urethra throughout its entire circumference. In most cases of this type, the fusion of the valves anteriorly is not complete. Slight separation of the folds exists at this point. In the second type there is a more or less cylindric ridge similar to that found in the preceding type, with the exception that it passes over the upper aspect of the verumontanum toward the internal sphincter. It divides into two forklike processes, which continue as membranous sheets and are attached to the urethra outside the internal sphincter. The third type has been found at different levels of the posterior urethra and apparently does not bear any relation to the verumontanum. It is similar in shape to the iris of the eye. This obstruction is attached to the inner circumference of the urethra, there being a small opening in the center.

The symptoms may be those brought about by local obstruction to urination, or from the backpressure on the kidneys producing renal injury, insufficiency and uremia. There may be dribbling, frequency, and incontinence, of the type which results from the overflow of a distended bladder which never becomes completely emptied.

Careful abdominal examination should be made to determine whether the bladder, ureters and kidneys are palpably dilated. Instrumentation of the urethra should be carried out delicately to detect the valves, to note the position, and, if obstruction is met, to find the instrument, generally a small pointed urethral catheter, which can be passed through the slit between the valves to catheterize the bladder. Cystoscopic examination should be carried out as soon as the condition of the patient permits. By careful manipulation of a child's small cystoscope, the slit between the two valves can usually be penetrated.

Practically the same preparatory treatment is necessary in these cases of prostatic urethral obstruction as in cases of prostatic hypertrophy with marked backpressure and much residual urine. Drainage should be maintained until the drop in nonprotein nitrogen and increase in output of phenolsulphonphthalein are sufficient to warrant the slight operation necessary to remove the valves.

A number 7 French punch instrument is passed into the urethra, and, by careful manipulation, through the aperture between the valves

53. Young, H. H., and McKay, R. W.: Congenital Valvular Obstruction of the Prostatic Urethra, *Surg. Gynec. Obst.* 48:509, 1929.

and on into the bladder. The bladder is then washed out and filled again with a weak antiseptic solution. Only one valve is removed at the first operation. If the obstruction has not been completely relieved, it may be advisable to make another cystoscopic examination to determine the presence of a remaining valve and to make an additional cut with the punch instrument on the opposite side. Fulguration was first carried out by means of the high frequency current and a ureter-catheterizing cystoscope, the valves being destroyed by fulguration. The prognosis depends largely on the extent of the obstruction, the character of the renal impairment, and the general condition of the patient.

Young and McKay reported twenty-one cases of a congenital valve of the posterior urethra observed at the Brady Urological Institute, in fifteen of which operation had been performed successfully. Nine of the patients were less than 16 years of age. The authors reviewed forty-one cases from the literature, in twelve of which operation was performed.

Diverticulum.—Gorowitz⁵⁴ stated that diverticula of the urethra in females are not congenital. They occur late in life by the influence of various mechanical, traumatic or inflammatory acquired factors. They often remain latent for a long period and become manifest through secondary conditions, such as infection, inflammation, and sometimes disease of the bladder. Palliative treatment is unsatisfactory; the best results are obtained by operation.

Stricture.—Campbell⁵⁵ reported a study of 1,244 cases of stricture in the urethra of the male. He concluded that more than 90 per cent of such strictures are of inflammatory origin, and that the condition depends on the severity of the urethritis rather than on the duration. Usually the strictures are multiple clinically, although they may be single pathologically. Traumatic strictures are usually single. Nephropathy secondary to obstruction by stricture is of significance. The author treats stricture on the basis of renal injury and infection. Dilatation is the nonoperative or palliative treatment, and its employment must be persistent and prolonged. The indications for operation are failure of response to dilatation, and certain complicating infections. Strictures of the pendulous urethra and scrotal bulb are cut by internal urethrotomy, preferably under spinal anesthesia. An indwelling catheter provides drainage of the bladder and checks bleeding. For deeper strictures perineal section is usually necessary, in which case a perineal bladder tube should always be used. Extensive multiple

54. Gorowitz, P.: Ueber Divertikel der weiblichen Harnöhre, Ztschr. f. Urol. 22:183, 1928.

55. Campbell, M. F.: Stricture of the Male Urethra, Ann. Surg. 89:379, 1929.

strictures may require both external and internal urethrotomy. Dilation with sounds, beginning from seven to ten days after urethrotomy and continuing every five or ten days thereafter until the canal maintains a normal caliber, should be performed, with rare exception. Numerous postoperative complications may develop, many of which are potentially fatal. The immediate mortality is about 5 per cent. Most patients are improved by operation. A third will require reoperation, two thirds of these within ten years. Gentleness is a prime consideration in all urethral instrumentation. Campbell stated the belief that it is of greater importance than asepsis.

Flandrin⁵⁶ stated that suprapubic drainage, which is so frequently resorted to in cases of traumatic rupture of the urethra, hypospadias, and resection of traumatic strictures, has given, in Legueu's service, excellent results when used as the first-stage operation in cases of complicated stricture of the urethra. Flandrin gave the following indications for its use: strictures which render catheterization difficult and which are accompanied by distention of the bladder; tight and multiple strictures associated with extensive urethral infection and balanitis; tight and hard strictures accompanied by localized subacute periurethritis, and tight and hard strictures, with fistulous or nonfistulous chronic periurethritis.

TESTES, EPIDIDYMIS AND SEMINAL VESICLES

Undescended Testes.—Higgins and Welti⁵⁷ stated that statistics compiled by various authors agree regarding the frequency of undescended testes. Marshall reported an incidence of 1.02 per cent in 10,800 men examined. Ziebert, in examination of men for the Austrian army, reported 14,057 cases among 6,962,543 men, an incidence of 0.2 per cent.

Faulty descent of the testis occurs most commonly on the right side. Grossly, the undescended testis is usually smaller, less elastic, and less firm in consistence than is a normal testis. Ombrédanne observed that before puberty an ectopic testis looks, on section, like a normal child's testis. Its epithelial cells are normal. The interstitial cells are proportionately more numerous than those of an adult's testis, but this is normal in a child. After puberty the interstitial cells are numerous, which is an argument against orchidectomy, if it can be avoided. Only a few spermatogones are found after puberty, rarely spermatids, and never spermatozooids. If an operation is to be useful,

56. Flandrin, P.: La cystostomie hypogastrique temporaire dans le traitement des rétrécissements compliqués de l'urètre, Paris méd. 69:335, 1928.

57. Higgins, C. C., and Welti, H.: Surgical Treatment of Undescended Testicles, Surg. Gynec. Obst. 48:536, 1929.

it must be done before puberty because at that time the testis is normal and it can be hoped that if the testis is placed in a normal position it will grow normally.

Of 452 cases of malignant growths of the testis reported by Cunningham, 412 occurred in normally placed testes. Ombrédanne pointed out that, although a malignant growth is frequently observed in these cases, it occurs only in adults. Torsion may also occur, especially in cases of so-called migrating testes. In these cases, because of a congenital deficiency in the internal oblique muscle and its conjoined tendon, the testis can more readily be moved upward and downward. The association of an undescended testis with hernia has long been recognized. In a series of 80,736 cases of hernia there were 1,357 undescended testes. Atrophy results if the testis is not restored to the normal position.

There are various opinions as to the correct age for operation. It should be done before the age of puberty is reached, and preferably between the ages of 8 and 12 years. If by manipulation the testis can be brought to the bottom of the scrotum, operation is contraindicated, since under these circumstances descent will always occur at the age of puberty. If the testis cannot be found clinically, operation is indicated.

Higgins and Welti performed transscrotal orchidopexy, a procedure which has been performed by Ombrédanne for twenty years in many hundreds of cases. The usual incision for inguinal hernia is made, and the anterior wall of the inguinal canal is incised. The cord is then exposed and isolated. The canal is explored. A radical operation for hernia should be performed at this stage. If the canal is not occupied by a hernia, obliteration of the canal is not necessary, since it will close spontaneously after operation if the wall of the inguinal canal has been restored in front of it. A sliding knot is then placed above the gland and the testis is covered with a warm compress. The scrotal raphe is marked with two clamps and is held gently. With the left index finger, a passage is made into the scrotum, beginning at the inguinal incision, and progressing toward the middle of the sac diagonally opposite. When the elastic septum is reached, it is forced back and the skin of the scrotum on the opposite side is raised. On the side of the scrotum elevated by the index finger, a vertical incision approximately 3 cm. in length is made. The septum becomes visible, being recognized by its white color. By means of a compress the two cutaneous lips are pushed back along the finger which is pushing the septum in the inverse direction. Separation is thus accomplished and a place for the testis is secured. The septum, which has been elevated by the index finger, is pushed back, is grasped above and below, and is then incised vertically between clamps. The free ends of the catgut,

the slip-knot of which has been placed around the neck of the gland, are grasped and brought through the opening in the septum.

[COMPILERS' NOTE.—In this country the operations of Bevan and of Torek for undescended testes have been much in vogue during the last few years, and the operation of Ombrédanne seems to have been seldom used. As described by Higgins and Welti, this operation has the advantage of being a one-stage procedure, so far as each side is concerned, and is more easily applied if the vas deferens is short. The excellent results reported seem to indicate that the Ombrédanne technic is worthy of trial.]

Tuberculosis.—Hinman⁵⁸ stated that one of the prominent characteristics of genito-urinary tuberculosis is its tendency to spread from one part of the tract to the other, regardless of whether the primary lesion is in the urinary or genital tract. Renal tuberculosis in the male is more common than genital tuberculosis, the average incidence of which is 0.5 per cent, whereas that of renal tuberculosis is estimated as from 1 to 5 per cent.

Of Hinman's fifty-one cases of genital tuberculosis, only twenty (39.4 per cent) were primary in the genital tract; the others were associated with active tuberculosis elsewhere in the body. A significant clinical fact in the treatment of renal tuberculosis is that the infection begins in one kidney and is manifested in the other kidney in the late stages of the disease except in cases of a miliary type. Early nephrectomy is the treatment of choice to prevent extension of the disease to other parts of the tract.

Whether the primary lesion in genital tuberculosis occurs in the epididymis or seminal vesicle and prostate gland is still a controversial subject. Those who maintain that the primary focus is in the epididymis point out that primary tuberculous epididymitis is frequently observed to occur independently, whereas if genital tuberculosis exists, the whole tract is generally involved, the spread being from the primary lesion in the epididymis. The extent of a lesion cannot be taken as an indication of its duration; involvement of the opposite epididymis may be hematogenous. Lesions in the epididymis may have been overlooked in cases in which the lesion was supposedly in the prostate gland and the bladder primarily. In the majority of cases simple epididymectomy effects improvement or arrest of the lesion recognized clinically as in the bladder and in the prostate gland. Tuberculosis of the seminal vesicles and prostate gland is rarely recognized in the absence of involvement of the epididymis. The presence of tuberculosis in the seminal vesicles or prostate gland, as indicated by the

58. Hinman, Frank: The Surgical Treatment of Lower Tract Tuberculosis, Genital and Vesical, J. Urol. 20:521, 1928.

presence of nodules, without evidence of disease in the epididymis, is more common. Tuberculous epididymitis rarely occurs alone, and it is often preceded by symptoms of vesiculitis or prostatitis. Whenever the epididymis is affected by tuberculosis, the initial lesion is in the globus minor; the globus minor is also first involved when the disease spreads to the opposite epididymis. From the globus minor it extends to the body and globus major, making a 100 per cent involvement of the globus minor. Pathologic facts supporting the belief that the lesion is primary in the seminal vesicles or prostate gland are: (1) lesions of the epididymis alone are rarely found at necropsy, whereas tuberculous lesions of the seminal vesicles and prostate gland unaccompanied by lesions in the epididymis are frequently reported; (2) in cases in which the disease affects the whole genital tract, the lesions in the seminal vesicles and prostate gland generally have the appearance of being more advanced and older, and (3) lesions in the globus minor of the epididymis appear to be older and more advanced than those of the body or globus major.

Hinman observed seventeen cases of epididymitis without clinical evidence of vesiculitis. In eleven cases simple epididymectomy was performed; in six cases the treatment was nonsurgical. Five patients were not traced. Of those operated on, four had bilateral epididymectomy, four had right epididymectomy and three had left epididymectomy. Three of these eleven patients have had nephrectomy, and three have been lost from observation. Four patients, eight, seven and three years and five months after operation, stated that they were better than before surgical treatment. Three patients died after leaving the hospital, two of tuberculosis and the other apparently of acute pneumonia. Of the six patients not treated surgically, two had left nephrectomy subsequently. One of the remaining four patients was heard from four years after examination, and at that time his general condition was good. One patient was not traced, and two patients are dead, both of tuberculosis. To summarize, of the twelve patients who were traced six are alive and six dead, three of whom had had epididymectomy.

Hinman observed a second group of seventeen patients in whom the seminal vesicles showed clinical evidence of involvement. Five were treated by epididymectomy, and twelve were not treated surgically. Nine patients were traced; six were alive and three were dead. Five of the nine had had simple epididymectomy, which was bilateral in four. Two patients were improved four and six years after operation, two were worse, and one died of embolism six days after epididymectomy. Of the twelve patients not treated surgically, four had evidence of bilateral tuberculous epididymitis, one patient had evidence of right epididymitis, and three patients of left epididymitis. The four remain-

ing patients with involvement of the seminal vesicles did not show evidence of involvement of the epididymis. Six patients also had urinary tuberculosis; three showed evidence of tuberculosis in both kidneys; two in the right kidney alone, and two in the left kidney alone. Four of these had vesical involvement.

In a third series there were thirteen patients with tuberculosis of the entire genital tract. Radical bilateral epididymectomy, vasectomy, seminal vesiculectomy, and in some cases partial prostatectomy were performed. Two of these patients were dead, both were poor surgical risks, two had not been traced, and nine were living and well. The results in these nine patients have been satisfactory except for a perineal sinus which persisted for months to a few years in cases in which partial prostatectomy was performed.

Tuberculous ulceration of the bladder is common in both renal and genital tuberculosis. Of 148 patients with genito-urinary tuberculosis, 110 had cystoscopic evidence of active tuberculosis of the bladder. After removal of the primary focus in the genito-urinary tract, the lesions of the bladder often healed spontaneously.

Hinman concluded that there are two clinical types of genital tuberculosis: (1) that in which the more advanced or only lesion is in the epididymis, and (2) that in which the seminal vesicles are involved with or without epididymitis. If the primary focus is in the epididymis and not associated with active lesions elsewhere, the indication is for epididymectomy, and if the seminal vesicles are involved the radical operation should be performed.

Eisenstaedt⁵⁹ found that it is possible for a patient to have right epididymitis of tuberculous origin, the left half of the prostate gland being involved by tuberculosis and possibly the right orchis. He had been successful with treatment by the roentgen ray, and operates only if necrosis and secondary infection necessitate drainage.

Süssig, working under Ghon in Prague in 1921, examined between 130,000 and 180,000 serial sections in cases of urogenital tuberculosis. He found that in the majority of cases the term, primary, could not be accurately applied, even if it was confined to the urogenital tract. The bacteria were found in multiple portions of the urogenital tract in many of the cases.

McKenna,⁶⁰ in 104 postmortem examinations in a comparative study of tuberculosis of the genito-urinary tract, found eight cases of primary lesions in the epididymis and three in the prostate gland and vesicles, showing that they occurred two and a half times more commonly in the epididymis than in the prostate gland or vesicles. He noted that

59. Eisenstaedt, J. S.: Discussion, *J. Urol.* **20**:539, 1928

60. McKenna, C. M.: Discussion, *J. Urol.* **20**:539, 1928.

patients suffering with tuberculosis of the epididymis, vesicles or prostate gland do well if they are treated by tuberculin and the direct rays of the sun.

UROLOGIC SURGERY

Hunt⁶¹ reported that at the Mayo Clinic during 1928 there were 881 operations on the kidneys, ureters and bladder, with thirty-four deaths, a mortality rate of 3.8 per cent. In 117 operations for malignant lesions, there were eleven deaths (9.3 per cent), whereas in 764 operations for benign disease there were twenty-three deaths (3 per cent).

Lithiasis was the predominating lesion of the kidney, for which there were 133 operations without a death. Infection and destruction of renal tissue were so marked that nephrectomy was necessary in forty-seven cases (33 per cent). Pelviolithotomy was utilized in the removal of single and multiple stones from the kidney in 87 per cent of the cases. During the last two years pelviolithotomy and nephrolithotomy have been performed in 164 cases without mortality. Nephrectomy was performed in 200 cases: for renal tuberculosis in fifty-two cases, for nephrolithiasis in forty-six, for hydronephrosis in forty-three, for pyonephrosis in seventeen, for pyelonephritis in twelve, for a malignant growth in twenty-seven, for multiple cysts of the kidney in two, and for rupture of the kidney in one case. There were five deaths following nephrectomy.

The malignant lesions of the bladder are most formidable; approximately only 50 per cent of the lesions are operable. Palliative suprapubic cystostomy is sometimes used in cases of inoperable lesions, and these contribute considerably to the mortality of cystostomy for the various conditions in which it is necessary. Operations were carried out in thirty-two cases. The procedures of choice for lesions of the dome and the posterior lateral walls of the bladder are segmental resection and excision, and in lesions of a low grade of malignancy they have been productive of the best results. Surgical diathermy is being used with considerable success in lesions of the base of the bladder with involvement of one or the other ureter. Disposition of the ureters is a significant problem because one or both ureters are usually dilated and unsuitable for transplantation into the sigmoid.

Diverticula of the bladder have been removed in twenty-four cases. In most instances they were large, were associated with prostatic obstruction, and were removed preliminary to prostatectomy.

There were 265 prostatectomies, of which 249 were for benign prostatic hypertrophy and sixteen for malignant disease. There were

61. Hunt, V. C.: Report of the Major Surgical Procedures on the Kidney, Bladder and Prostate at the Mayo Clinic for 1928, Proc. Staff Meet. Mayo Clinic 4:86, 1929.

twelve deaths in cases of benign prostatic hypertrophy (4.8 per cent). Perineal prostatectomy was done in nine cases, with excellent recovery in all. The other patients were all operated on by the suprapubic method; the one-stage operation was employed in 69 per cent of the cases. Those patients who had had preliminary cystostomy recovered from the condition requiring cystostomy and arrived at a stage of improvement so that prostatectomy was undertaken as a second step, with a mortality of 3.9 per cent. For the year the mortality was 4 per cent following preliminary cystostomy performed as the first step of two-stage prostatectomy, as a result of the poor condition of the patients at the time that cystostomy was necessary. The average age of patients who died following simple cystostomy preliminary to prostatectomy was seventy-seven years.

In prostatic surgery, age is an important factor in mortality rate and should be considered in determining the advisability of prostatectomy and the methods of procedure. In a review of 1,973 prostatectomies, with nearly as many patients more than 65 years of age as there were less than 65 years, a definite relationship between age and mortality rate was established. The average mortality before the age of 65 years was 3.9 per cent; after 65 it was 6.3 per cent. The rate rises rapidly after the age of 70, which emphasizes the necessity for most careful consideration of prostatic obstruction in the aged.

CHYLURIA

Wood⁶² reported a case of chyluria which originated in the left kidney. Examination did not reveal eosinophilia, or parasites or ova in the blood, urine or stools. The chyluria first occurred at the age of 15 and cleared up without treatment. It recurred at the age of 71 years. The differential phenolsulphonphthalein tests showed the output of the left kidney to be more than that of the right on account of right-sided nephrosis. A pyelogram of the left kidney revealed an apparent communication between the extrarenal pelvis and the aortic lymph nodes in the vicinity of the pelvis. Such a communication was not observed on the right side. The chyluria ceased after pyelography, without other treatment, and the condition has not recurred.

LABORATORY TECHNIC

Blanc⁶³ reviewed his method of making a phenolsulphonphthalein test; he injected 4 cc., representing 6 mg. of the product; 70 per cent of this should be eliminated in an hour and ten minutes. From the

62. Wood, A. H.: Unilateral Renal Chyluria, *J. Urol.* 21:109, 1929.

63. Blanc, H.: Les lois de l'élimination de la phéno-sulfophtaléine; leur valeur en chirurgie urinaire, *Paris méd.* 69:331, 1928.

numerous tests which he carried out, he drew several conclusions. The rate of phenolsulphonphthalein of separated or total urines has a great value by itself, as far as an absolute rate is concerned, without considering the amount of urine excreted during the time of exploration. The rate of elimination of the phenolsulphonphthalein represents exactly the functional value of the renal parenchyma, but it is not necessarily a measure of the anatomic value nor of the function of the tubular apparatus. It constitutes an expression of the physiologic value more than the anatomic value. It decreases proportionately with the distention or the destruction of the kidney. In cases of healthy kidneys the rate of output of phenolsulphonphthalein in total or separated urines remains about the same, regardless of the time the urine has been collected. In cases of healthy or diseased kidneys, without any lesions of the active glandular cells, the output of phenolsulphonphthalein remains constant as long as the functional value remains constant. If a diseased kidney shows loss of function and diminution in elimination of the phenolsulphonphthalein, the other kidney will increase elimination. On separated urines, there usually will be a parallelism between the uric acid and the excretion of phenolsulphonphthalein. Each functional change which the renal parenchyma undergoes, except in the presence of a long-standing lesion, influences the return of phenolsulphonphthalein.

Cambridge and Howard⁶⁴ carried out experiments to find an improved method for titrating sugar in urine and blood. *They considered that the methods ordinarily used are too inaccurate or difficult to carry out, except after considerable experience. They use arsenious acid, which is stable in dilute solutions, rather than sodium thiosulphate, which deteriorates rapidly, and they follow the method of Melli for the estimation of calcium. Arsenious acid also gives a readily recognizable and critical end-point.

They consider the advantages of their methods to be that all the solutions are stable and keep for an indefinite period in well-stoppered bottles, that the use of a regulated gas supply is avoided, that a sharp and easily recognized end-point is obtained in the titrations and that accurate results may be secured even by inexperienced workers.

UROLOGY AND GYNECOLOGY

Bonney⁶⁵ stated that since the branches of gynecology and urology are so closely associated, specialists in these branches should be reasonably well informed of the work of the other.

64. Cambridge, P. J., and Howard, H. A. H.: An Improved Method for Titrating Sugar in Urine and Blood, *Brit. J. Urol.* 1:17, 1929.

65. Bonney, Victor: Urology in Relation to Gynaecology, *Brit. J. Urol.* 1:23, 1929.

It is important to have a thorough understanding of the supporting structures of the pelvis, consisting of the cardinal ligaments and the pubocervical fascia. The bladder rests on this fibromuscular shelf, and any alteration in it affects the bladder. There are three common deformities affecting this shelf. In the first deformity, the pubocervical fascia buckles or hammocks downward to produce a cystocele. The effect on the bladder is difficulty in passing urine and failure completely to empty the bladder. In the second deformity the attachment of the pubocervical fascia at its anterior end becomes weakened, so that, on straining, this end of it droops, which results in interference with the sphincteric mechanism of the bladder. Some form of incontinence results and is produced on effort, such as sneezing, coughing or running. The third deformity is the retroversion of the whole pelvic shelf, so that the line of the vaginal axis protracted beyond the upper end of the canal would strike the sacrum somewhere about its second piece. The vagina retroverts with the shelf, and the bladder moves backward with both of them. It is important to recognize this deformity because of the fact that cystocele is often wrongly diagnosed; pouching of the bladder does not occur in these cases.

In abdominal operations Bonney observed that the more marked the postoperative intestinal symptoms, the more profuse is the bacterial infection of the urine, so that pyelitis in some degree is common. The infection does not always disappear with the healing of the operative area, but may continue for months or years afterward. Postoperative ureteric fistula following the Wertheim operation for carcinoma of the cervix is the result of sloughing of the ureter several days after operation, which leaves from 5 to 7 cm. of these conduits running free across the pelvis. Bonney successfully grafted the ureter into the bladder in many of these cases, a procedure which was made easier because the ureter is always dilated above the point of leakage. Nephrectomy is a hazardous procedure, but there are some cases in which it is necessary, particularly those in which the fistula had existed so long that the kidney on that side is disorganized.

Infection of the vagina by the streptococcus, which is relatively common, may sometimes be an overlooked source of streptococcal urinary infection.

Pyelitis of pregnancy is generally held to be due to the pressure of the enlarging uterus on the ureters. Pelvic tumors other than that of pregnancy rarely cause pressure on the ureters sufficient to obstruct them, even when the tumor is tightly impacted in the pelvis. Innocent growths such as fibromyomas or ovarian cysts rarely affect the ureters, but they may have a marked effect on the bladder, particularly fibromyomas. One of the earliest symptoms of this is increased fre-

quency of urination. An impacted fibromyoma is one of the most common causes of retention of urine among women.

[COMPILERS' NOTE.—The importance of a closer relationship between the urologist and gynecologist is constantly being emphasized, a point which many gynecologists, notably those from the Kelly school in Baltimore, have insisted on for many years.

The changes in the urinary tract incident to gestation, the proximity of the urinary and generative tracts in women, the easy access of the streptococcus or the colon bacillus to the bladder, and the stasis due to pressure changes brought about from pelvic enlargements, frequently force the gynecologist into a detailed urologic study which is enlightening from the standpoint of diagnosis, treatment and prognosis. Whether or not the gynecologist shall be his own urologist is a moot point. It would seem to be common-sense reasoning that this should be determined by the special training and the inclination of the individual surgeon and that a sharp line of demarcation should not necessarily be drawn between the specialties in practice. Every one who professes to be proficient in either specialty should have a reasonable understanding of the fundamental principles involved in the practice of both gynecology and urology.]

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TRANSACTIONS OF THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

TWELFTH ANNUAL MEETING, ST. LOUIS
APRIL 25, 26 AND 27, 1929

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1919 ATLANTIC CITY, N. J., June 9
1920 NEW ORLEANS, May 1
1921 BOSTON, June 6
1922 WASHINGTON, D. C., April 29
1923 CHICAGO, May 28
1924 ROCHESTER, MINN., June 5
1925 WASHINGTON, D. C., May 4
1926 MONTREAL, P. Q., September 30
1927 NEW YORK, May 9
1928 WASHINGTON, D. C., April 30
1929 ST. LOUIS, April 25

REPORT ON THE ACTIVITIES OF THE CHEST TUMOR REGISTRY

During the past year the recommendations of the Council of the American Association for Thoracic Surgery relative to the establishment of a Registry of Chest Tumors have been carried out. Letters describing the Registry, together with a statement of the types of tumors to be included and registration forms for the submission of material, were sent to all members of the American Association for Thoracic Surgery, the American Surgical Association and the Association of American Physicians, and to the pathologists of the leading clinics of the country.

Up to date the actual number of cases registered has been small, but correspondence between the registrar and a number of surgeons interested indicates that a considerable number of cases are available and should be registered.

The registrar has purposely avoided too active solicitation of material, feeling that the success of such an undertaking depends, in part at least, on its obtaining the spontaneous support of those interested. However, at the suggestion of the Council of the Association, blank forms on which data regarding cases to be registered may be filled in will be circulated to facilitate the submission of material.

The Registry is designed to include all primary intrathoracic tumors and all such other tumors of the chest wall and thoracic vertebrae as impinge on the pleural cavity. The committee requests the cooperation of all interested persons in the registration of such cases.

WILLIAM DEW. ANDRUS, M.D., Registrar,
Cincinnati General Hospital, Cincinnati.

PULMONARY TUBERCULOSIS

PATHOLOGY AND TREATMENT *

JOHN L. YATES, M.D.

MILWAUKEE

There are approximately 625,000 people suffering from pulmonary tuberculosis in this country, 85,000 of whom will die within the year. The total time spent annually in combating the disease by those potentially and actually affected is about 633,333 years, and even so more than two thirds of them suffer one or more recrudescences after apparent recoveries. More than three-fourths are afflicted while their productive and earning capacities would be otherwise little, if at all, impaired. The total of the yearly costs of therapy, exclusive of consultation and attendance fees, and of the losses imposed by deaths after intervals of illness and by the duration and degree of temporary and permanent disabilities of those who survive will amount to \$870,000,000.

During the past fifteen years, although the population has increased, the annual death rate has been reduced from 155,000 to 85,000, the incidence from 1,000,000 to 625,000 and the costs by about \$250,000,000.¹

Progress made in combating pulmonary tuberculosis has resulted not only from a clearer perception of its pathology which provided a larger measure of prevention, earlier diagnosis, more effective treatment and after-care, but also from improved housing, schooling, and working conditions, better and cleaner food, more wholesome methods of living, and restricted emigration.

During the same interval, tuberculous cows had been eliminated from dairy herds in some communities. In them the incidence of tuberculosis of bones, joints and lymph glands was reduced to a small fraction of the previous numbers. The few persons who now develop these forms of tuberculosis are more seriously affected, some because of their greater susceptibility to bovine tuberculosis; others are infected with bacilli of the human type. Although other influences, such as greater attention given to teeth and tonsils, were contributory, the elimination of the most dangerous source of infection was the effective agency. Presumably the incidence of pulmonary tuberculosis has also been reduced in the same communities even though the reduction has not been demonstrated by statistics.

* Presidential Address.

1. Information from which these figures were obtained was furnished by Miss Aimee Weinstock and Mr. Leslie L. Lewis of the Wisconsin Anti-Tuberculosis Association, who made conservative estimates from the data at their command.

The need to hasten the curtailment of the social and economic burdens imposed by the white plague compels consideration of the chief obstacles to past and present progress. The foremost obstacle is incomplete knowledge of the influences that govern the inception and evolution of the disease. Next, is the lethargy born of satisfaction and subservience to established routinism that prevents application in practice of available knowledge, stifles investigation and assures mass treatment. Last, is the numbing effect of the procrastination that makes a majority of patients realize that nothing aggressive is or will be done to satisfy individual requirements until long after pacifistic therapy has been proved futile, frequently not until approaching death impels attempts to camouflage neglect.

A review of the biologic aspects of extrapulmonary tuberculosis will provide a clearer perception of pulmonary tuberculosis and show why the more effective means to prevention and treatment can be determined by physiology and pathology more accurately and promptly than by any other means.

EXTRAPULMONARY TUBERCULOSIS

INCEPTION

Three conditions are precedent to the inception and evolution of tuberculous processes. Tubercle bacilli must be deposited on the skin and mucous membrane and the peritoneum in females which form the surfaces of the body and are barriers against invasion. (The bronchial mucous membrane and the cells lining the alveoli of the lungs will be considered later.) Bacilli must become invaders of the body by passing these barriers. Once the barriers have been passed, the microbes must be sufficiently robust not only to survive temporarily but also sooner or later to develop parasitic activities.

INVASION

Few exceptions prove the rule that all people but some infants are carriers of virulent tubercle bacilli which have been deposited repeatedly on the surfaces of the body from the air, contacts and ingesta. So long as the bacteria remain under no pressure on a surface, they are innocuous.² Invasion of the body begins at a portal of entry in a

2. Normal external surfaces are the skin, mucous membrane, lining of pulmonary alveoli and the peritoneum in females. Normal internal surfaces are: the nutritional, formed by the endothelium lining the vessels of the systemic circulation; the ventilating, formed by the endothelium lining the vessels of the pulmonary circulation; the digestive, formed by the endothelium lining the vessels of the portal circulation; and the drainage surface, formed by the cells lining the lymph vessels. Abnormal surfaces are the deeper tissues exposed by injuries, the surfaces of ulcers and the inner surfaces of the walls of abscesses.

surface and continues by repetition of similar steps. Consideration of the destruction of most of the invading bacilli is omitted for the present to avoid complication.

Bacilli under pressure and those fixed by secretions or exudates enter, pass through or between intact surface cells, pass through superficial lesions or are carried across these barriers within wandering phagocytes. They may be retained in surface cells or at the surface of lesions and may or may not provoke inflammation which usually includes formation of tubercles. Inflammation is provoked by parasitic activities of bacilli, namely, the elaboration of noxious egesta and reproduction. Bacilli that survive but induce no inflammation are for that time saprophytes, i. e., they elaborate so little noxious egesta that adjacent cells are not overactivated and their reproduction suffices merely to prevent extinction.

Having passed the first barrier, they enter the subcutaneous or submucous tissues which constitute another barrier. (Direct contamination of the peritoneum of females is too rare to warrant consideration.) Here the bacilli are under tissue tension. They may be retained in and between cells and produce or do not produce lesions according as they are parasitic or saprophytic. Those deposited on the outer surface of the endothelial cells of blood and lymph capillaries may enter, pass through or between them. More often the bacilli are taken up by phagocytes and carried into the lymph vessels. The naked bacilli and those carried within phagocytes which have entered the blood and lymph streams have passed another barrier presented by the external vascular surfaces and are disseminated. As some dissemination is a prompt and constant consequence of invasion, tuberculosis even in its incipient stage and in its milder forms is a systemic contamination.

The bacilli, naked or within phagocytes, carried in the blood are deposited on the inner surface of the capillary endothelium. Many of those entering the portal circulation are retained in the hepatic capillaries in which the Kupffer cells are present. The others and nearly all of those entering the capillaries in the systemic circuit are carried to the lungs. The few that are not deposited on the walls of the capillaries in the lesser circuit, which will be discussed later, are disseminated in the arterial blood of the systemic circulation. They are deposited on the walls of its capillaries which form the nutritional surface of every organ and tissue in the body. Consequently, every structure is liable to invasion because these microbes may penetrate this barrier, the nutritional surface, just as they pass other barriers. The parenchyma of organs and the cells of tissue present another barrier analogous to the subcutaneous and submucous structures wherein again microbes may or may not provoke inflammation and from which they may or may not be disseminated.

Bacilli enter, pass through or between the cells lining the lymph vessels which constitute the drainage surface of all structures but the central nervous system, eye, internal ear and spleen which have no lymphatics. Bacilli carried in the lymph, whether naked or in phagocytes, are usually deposited on the endothelium of the sinuses in the proximal lymph gland to which they are carried, or they may pass through the sinuses of this gland and be deposited on the sinus walls of the next gland. In lymph glands, reticulo-endothelium forms part of the drainage surface and has a special capacity to engulf and to destroy bacteria. This barrier is less easily passed, but once bacilli have entered the parenchyma of the gland, there is the same sequence of events. The bacilli provoke lesions and are retained or disseminated through blood or lymph vessels or are disseminated or retained without provoking lesions. Ultimately, some of the bacilli that enter the lymph are delivered into the blood through the right or thoracic ducts. The many which penetrate the intestinal mucosa are delivered rapidly, especially during active digestion, into the receptaculum chylae and thence promptly into the blood. Bacilli carried in the lymph formed in tissues outside the digestive tract reach the blood after longer intervals. Not only have they farther to travel but the collateral pathways are fewer. The sinuses within tuberculous glands are often obstructed, and this compels the lymph in afferent vessels to seek unobstructed centrifugal channels which may carry lymph in devious channels through adjacent or even remote regions and thus lead to anomalous dissemination of bacilli but nearly always to lymph glands.

Summary.—The significant phases in the cycles of invasion of the body are:

First Cycle

- (1) Dissemination of bacilli through the air
- (2) Deposition of bacilli on a normal or abnormal external surface of the body from air, ingesta or contacts
- (3) Penetration of an external surface of the body
- (4) Deposition of bacilli within subcutaneous or submucous tissue
- (5) Provocation of or failure to provoke inflammation

Second Cycle

- (1) Dissemination of bacilli through blood and lymph
- (2) Deposition of bacilli on a normal or abnormal internal surface of the body
- (3) Penetration of an internal surface of the body
- (4) Deposition of bacilli within the parenchyma of organs or between the cells of tissues
- (5) Provocation of or failure to provoke inflammation

Subsequent Cycles

The first cycle is repeated in all those who survive infancy.

The second cycle is repeated in all those of less than high grades of insusceptibility, continuous in those of lower grades of susceptibility.

SURVIVAL OF TUBERCLE BACILLI WITHIN A BODY

The divers activities of cells are products of metabolism. Individuality of cell structure, the result of differentiation, determines the peculiarities of metabolism and therefore of function. The rate of production of function, i. e., the metabolic rate, is governed by the actions of excitatory and repressive influences and is limited by the capacity of cells to respond thereto, namely, by their strength and endurance.

Rates of metabolism and corresponding grades of activities are higher during the periods of exercise and lower during the intervals of rest that alternate throughout cell life. As cells weaken because of untoward alterations in their structure resultant from senility, the fatigue of over-exertion, the atrophy of underexertion, trauma, dehydration, malnutrition, starvation and intoxication, the rates of their metabolism in response to positive influences fall proportionately. If metabolism falls below a certain level, the limit of viability, and remains below the level for more than brief intervals, the cells are lethally injured. Death may occur at once. Sometimes the injuries which are progressive are less severe and lead to necrosis after considerable intervals during which some functions are produced.

The limit of viability is not fixed. It is lower if cell structure is stronger and more resistant and is also lower for all cells in a favorable than in an antagonistic environment.

Tubercle bacilli within the body of a host are in an antagonistic environment. In order to survive they must maintain their metabolic rates at or above a limit of viability which is higher than it usually is when they are on an external surface.

The pathogenic activities of bacilli are elaboration of noxious egesta and reproduction. So long as their metabolism is restrained by the antagonism of the host at viable limits the elaboration of noxious egesta is insufficient to provoke local inflammation, and reproduction only suffices to prevent extermination. In other words, under such conditions bacilli are saprophytes, living at the expense of the host but not being otherwise harmful. Indeed they may be beneficial despite some dissemination of organisms. Their noxious egesta, although not potent enough to provoke local reactions, supposedly arouse a measure of defensive systemic responses. There is no recognizable evidence of infection in this state, called latent tuberculosis. When the antagonism produced by the host is inadequate, the metabolism of the bacilli rises

above the limit of viability, and they become parasites. Elaboration of noxious egesta suffices to provoke local inflammation; bacilli reproduce more rapidly; both egesta and bacilli are so disseminated that obvious systemic responses occur, and other foci of infection are established.

Summary.—Tubercle bacilli, when they invade a body, enter an unfavorable environment.

They awaken more active antagonism by the actions of their noxious egesta that provoke local and systemic irritation and by the dissemination of bacilli.

In order to survive, the bacilli must maintain the rates of their metabolism at or above viable limits which fluctuate with the amount of antagonism offered by the host.

A majority of invaders succumb or are destroyed.

A proportion are able to maintain their metabolism at viable limits. They are saprophytes.

Saprophytes live at the expense of the host and produce latent tuberculosis.

Latent tuberculosis is harmless, possibly beneficial, so long as the bacilli are restrained in a state of saprophytism.

A proportion maintain the rates of their metabolism above viable limits. They are parasites.

Parasites produce focal and disseminated irritants and, so long as the rates of their metabolism are not reduced to or below viable limits, cause tuberculosis.

EVOLUTION

A majority of people are insusceptible to tuberculosis. The susceptibility of the minority is of divers grades and some organs and tissues are more liable to develop lesions than others. Since invasion of external surfaces and dissemination of bacilli, certainly to many, probably to all organs and tissues, occurs repeatedly, the insusceptibility of some persons and the relative insusceptibility of certain organs and tissues in the others are traceable to differences in the antagonism offered to the invaders.

Antagonism is the sum of the local and systemic responses to focal and disseminated irritants, which together produce resistance, defense and repair.

Resistance, defense and repair are produced by the activities of tissue cells adjacent to invading bacilli, supported, re-enforced and stimulated by the cellular and noncellular elements which emanate from the blood delivered to the structures invaded.

When resistance, which may be inherent or acquired, is adequate, the metabolism of invaders is restricted at or reduced below viable limits so promptly that manifestations of infection are undetectable. No

lesions, other than transient degenerations in contiguous cells, are provoked. Few bacilli are disseminated, and these are inactivated or destroyed with equal promptness wherever they are deposited.

Defense is aroused only if resistance is inadequate. Effective defense reduces the metabolism of bacilli to or below viable limits shortly but not until minimal lesions have developed. Noxious egesta and some bacilli have been disseminated. Manifestations of infection are slight but detectable. Meanwhile resistance is augmented rapidly, and the disseminated bacilli as well as those in the primary lesion are soon inactivated or destroyed. Less effective defense permits a longer duration of parasitic activities, the dissemination of more bacilli and noxious substances, and the development of larger primary and secondary lesions. Signs and symptoms of infection are unmistakable. Resistance is augmented gradually, and the disseminated bacilli are inactivated or destroyed, but not until some have produced manifest lesions in remote structures. Ineffective defense can but check the metabolism of parasites and thus retard the progressive development of lesions and the continued dissemination of noxious substances and parasites. Manifestations of infection increase in severity. Resistance is little augmented, and disseminated bacilli produce obvious lesions in several other structures, any one of which may be the cause of death instead of the initially preponderant lesion.

Repair begins with necrosis of tissue which results from destructive activities of parasites, and the injured tissue must be replaced if the disease is to be overcome. Cicatrization of minimal lesions impairs function immaterially. The scar is insufficient to be recognized intravital and can escape detection post mortem. Moderately large lesions, if repair is effective, are completely healed but the cicatrix impairs function. Even though defense suffices to arrest progress and repair is efficacious, some of the larger lesions are unhealed. The contents of abscesses, the rigidity of their walls or the fixation of the walls to unyielding contiguous structures prevent the collapse and approximation of the inner surfaces of cavities requisite to obliteration and complete cicatrization. Such lesions are to be differentiated from the progressive types that occur when defense is defective and are incompletely cicatrized because repair is inadequate.

Resistance, defense and repair, although they act somewhat in sequence in one focus of invasion, are acting *concertedly and constantly* throughout the body because disseminated invaders are present in numerous foci and subsequent invasion through external surfaces is repeated. The powers of resistance, defense and repair are prone to fluctuate similarly in the same person but have unequal values in different persons.

Local responses of tissue cells to invading tubercle bacilli are those incidental to acute, subacute and chronic types of inflammation plus the formation of tubercles. The efficacy of these responses in providing antagonism varies materially in the divers organs and tissues of one person, but the efficacy of the responses of the same structures in divers persons differs immaterially unless they have been injured previously.

Systemic responses are aroused by the presence in the blood of the noxious egesta of tubercle bacilli and the products of tissue degeneration which together constitute the toxemia of tuberculosis. Although every cell in the body can be affected, discussion will be restricted to the cells that form blood corpuscles, to those that contribute other than catabolic products to the plasma and to the myocardium.

Mother cells of the various blood corpuscles are inherently more or less robust. Later, when the inevitable tuberculous infection occurs, they will have become stronger or weaker, and their capacities to work under protracted stress are dissimilar. They all respond sooner or later to irritation (toxemia) by increasing the production of their specific functions, namely, a production of corpuscles above the usual rates. (Some of them also elaborate antibodies.) These unusual activities are continued until the irritation ceases with recovery or until the metabolism of the mother cells is reduced by fatigue and intoxication. Underproduction of functions by the weakened cells then succeeds overproduction, and in consequence the host is handicapped in proportion to the significance of the contributions of the corresponding corpuscles to the maintenance of life and to the production of antagonism.

Similarly, the cells that produce the usual constituents of the plasma, for example, those of the liver and of other structures concerned in digestion, of the glands of internal secretion,³ reticulo-endothelium, etc., are inherently more or less robust and more or less subject to fatigue and exhaustion. Similarly, too, if their metabolism is curtailed, their products are impaired quantitatively or qualitatively, and the untoward consequences are commensurate with the contributions of their usual products to survival and of their unusual products (antibodies) to antagonism.

The constituents of the blood are far more efficacious than the activities of tissue cells in producing antagonism to invading bacilli. Whatever structures are primarily invaded, untoward alterations in some constituent or constituents of the blood, revealed by repeated blood counts and estimations of sedimentation rates, are constantly present at the onset of tuberculosis. Thereafter the alterations parallel the course

3. Hyperthyroxinemia is constant in active tuberculosis, and the thyroid gland is prone to undergo degenerative changes in consequence of overwork and of toxemia.

of the disease. They become more favorable during improvement and not only disappear with recovery but are replaced with unusually favorable alterations which, if protracted, confer immunity. They grow progressively unfavorable as the disease progresses and commonly amount to cachexia as death approaches. Moreover, measures that improve the quality and increase the quantity of blood in circulation, particularly of that portion delivered to lesions, foster healing and other measures that remove lesions or promote their healing introduce improvement in the blood.

Those who are insusceptible to tuberculosis are able to make blood of proper quality in adequate quantity and to deliver it equably throughout their bodies under appropriate pressures. Their insusceptibility will endure so long as they retain those abilities. On the other hand, the susceptibility of the balance is proportionate to the deficits in those abilities, which are increased by age, unwholesome methods of living and disease. Hence, wholesome methods of living, viz., rest, recreation, avoidance of morbid emotions, ample well balanced diets, temperance, outdoor exercise, sunshine and energetic devotion to suitable occupations which favor formation and delivery of blood are invaluable agents in prophylaxis and in treatment.

Blood-forming units include the lymphatic and extralymphatic units; namely, the bone-marrow, intravascular and interstitial reticulo-endothelium, glands of internal secretion and all structures, such as the liver and digestive tract, which add to the plasma substances other than waste products. The component cells of the units are inherently more or less robust. Could an organism exist shielded from the unusual stresses imposed by hemorrhage, overexertion and disease, some of the cells would be incapacitated by senility before others, and this incapacity, even were there no other causes, would limit the life of the organism because all constituents of the blood are to some extent essential to longevity.

Inevitable unusual stresses hasten the incapacitation of the less virile blood-forming cells, and the consequent handicaps imposed on the organism are determined by the rôles played by the elements the cells contribute to the blood, to healthful existence, and to resisting pathogenic influences.

All constituents of the blood are more or less requisite to the provision of an effective antagonism to invading microbes. Antagonism to parasites that provoke acute processes or acute exacerbations of chronic processes is produced largely in the units within the bone-marrow and seldom provides lasting immunity. Antagonism to those arousing chronic processes is more from the lymph glandular units and, if effective, confers immunity. Certain parasites, e. g., *Streptococcus scarlatinæ*, and sometimes the tubercle bacilli, provoke inflammations that are initially acute and, if the host survives, later become chronic. Antagonism emanates at first more from the units in the bone-marrow, later from those in the lymph glands which, if efficacious, confers immunity.⁴

4. Yates and Raine, in Lewis: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1929. vol. 3, chapter 9.

Noxious egesta produced by invading tubercle bacilli are disseminated and produce what, in effect, is a toxemia. Every blood-forming structure in the body is thus irritated. If they are robust and the irritation suffices to provoke responses, they become unusually active and so continue until irritation ceases or they are progressively inactivated by fatigue, exhaustion, dehydration, malnutrition and intoxication. The consequences of overactivity are increments in the production of most of the corpuscles and of the usual constituents of the plasma, notably thyroxin, and the addition of protective substances which tend to reduce the metabolism of tubercle bacilli and to neutralize their noxious egesta.

The results of the earlier overactivities of the blood-forming structures and, if the disease progresses, of the subsequent lessened activities, are revealed by repeated examinations of the blood.

Early there is frequently a moderate polycythemia, later erythrocytopenia, and deficits in hemoglobin progress to cachexia.

Neutrophilia is present if the onset is acute, during acute exacerbations, in the terminal stages, and, as Medlar⁵ has indicated, is seldom attributable to coincidental infection with pyogenic bacteria.

Eosinophilia, usually a late manifestation, occurs if there is a considerable necrosis of lymph gland tissue or of lymphocytes (Bunting).

Basophils are little affected.

An early actual or relative lymphocytosis is the rule; later, as the disease progresses, lymphopenia increases. If the larger immature lymphocytes are in excess, the lymphoblasts are overworked, and is a less favorable response than when small mature lymphocytes are produced.

A moderate monocytosis is quite constant and betokens the response of the reticulo-endothelium to irritation which is unwholesome when these cells are overproduced or, as sometimes happens, are underproduced.

The rate of production of both lymphocytes and monocytes is indicative of the nature of the responses of the lymph gland units throughout the body and of the extralymphatic reticulo-endothelium which contribute the larger portion of the antagonism to tubercle bacilli. During intervals of health the number of lymphocytes and of monocytes produced bear a fairly constant ratio. Cunningham and Tompkins^{5a} have showed that this may be expressed graphically and also numerically by dividing the number of monocytes by the number of lymphocytes. The normal quotient is 0.3. If this observation be applied to patients suffering from tuberculosis, quotients in excess of 0.3 are less favorable and quotients below 0.3 are more favorable indexes. Fluctuations in these quotients occur during positive and negative phases of the disease and are of little significance if estimated from one count. If repeated counts are made and the ratios are quite constantly above 0.3 or below it, this is a factor in establishing a less favorable or a more favorable prognosis.

Protective substances are the most significant defensive constituent of the plasma. Their production seems to be nearly equivalent to the formation of the other constituents, and they contribute essentially to antagonism. The quality and quantity of protective substances in the blood cannot be determined directly, but they can be estimated indirectly since they vary inversely with rates of sedimentation. Early in the evolution of tuberculosis, sedimentation rates are abnormally rapid, less rapid if the antagonism is higher. If the disease progresses, they become correspondingly more rapid, particularly during exacerbations. Con-

5. Medlar: *Am. J. M. Sc.* **173**:824, 1927.

5a. Cunningham and Tompkins: *Am. Rev. Tuberc.* **17**:204, 1928.

trarily, if there is regression of the disease, the rates of sedimentation are slower; with and after recovery they are slower than normal.

Increments in basal metabolism during the active phases of tuberculosis and the degenerations noted post mortem in the thyroid glands of many patients who succumb to the disease indicate at once the constancy of hyperthyroxinemia during the more active phases of the malady and the importance of the contribution of the thyroid gland to antagonism.

The first step in the pathogenesis of tuberculosis is penetration of an external surface of the body, which occurs more often in the mucosa of the digestive tract.

All varieties of tuberculosis are systemic infections which develop because deficits in the blood permit invading bacilli to maintain their metabolism above viable limits. They differ solely in the location of predominant lesions, i. e., in skin, bone, central nervous system, lungs, lymph glands, spleen, digestive and genito-urinary tracts, serous cavities, fasciae, etc.

Except the delivery of bacilli to lymph glands in the lymph, to the liver in the blood of the portal circulation, pulmonary infections and those due to extension as from tuberculous tubes and intestines to peritoneum, all but surface structures are invaded by bacilli transported in the arterial blood of the systemic circulation, and liver, lungs and lymph glands may be thus infected. They are deposited on the endothelium of arterioles and capillaries which forms the nutritional surface of the body.

The number of bacilli present in the systemic arterial blood at any time is only large during the interval preceding the development of generalized miliary tuberculosis. The total number present throughout a lifetime is so large, because of repeated invasions of the body, that bacilli are deposited at one time or another on the nutritional surface of every structure and many times on some of them.

At the time of invasion of organs and tissues and during pathogenesis the quality of blood they receive is the same, though the quantity of blood and the extent of their nutritional surfaces vary greatly. Why then is tuberculosis relatively uncommon in some structures having a plentiful blood supply (brain, muscle, thyroid) and relatively common in others (kidney, liver, spleen)? Why is fascia lata so seldom affected?

Structure and function differ widely. Some structures are the more often subject to physical injuries, others to injuries inflicted by disease. It is unlikely that the nutritional surfaces are equally penetrable. Although the responses of tissue cells are less effective than the elements derived from the blood, nevertheless their contributions to antagonism are not only significant but also dissimilar and peculiar.

Organs that abstract chiefly water, salts and nourishment from the blood (thyroid, brain, muscle) are less prone to invasion than those

concerned in digestive, eliminative and defensive processes (liver, kidney, spleen), which withdraw additional substances. Peculiarities are exemplified in bones and lymph glands which are particularly susceptible to tubercle bacilli of the bovine type and quite as insusceptible to those of the avian type. Fibrous tissue, whether normal or cicatricial, is barren soil for bacilli. Hence the infrequency of fascial tuberculosis. The increased susceptibility of structures that have suffered previous injury which has resulted in some scarring is not attributable to the presence of fibrous tissue per se but to the reduction in blood supply.

Longevity depends on myocardial integrity. Myocardial weakness is revealed particularly by prolonged stress. Heart muscle is peculiarly vulnerable to the noxious egesta of tubercle bacilli and to the products of tissue degeneration they provoke.

Summary.—Inherent and acquired susceptibility and insusceptibility and the grades of susceptibility and insusceptibility are proportionate to lesser or greater degrees of antagonism offered by hosts to bacilli that have become invaders by having penetrated an external surface of their bodies.

Antagonism is the product of local and systemic responses to focal and disseminated irritations which together constitute resistance, defense and repair.

Adequate resistance confers insusceptibility. Invading bacilli are suppressed so promptly that there are no evidences of infection and the slightly degenerative lesions are evanescent.

Inadequate resistance and effective defense and repair that develop promptly lead to an early suppression of bacilli, but there are manifestations of infection though the lesions are minimal and the cicatrices too slight to impair function.

Less effective defense permits primary lesions to become larger before bacilli are suppressed; secondary lesions are often recognizable. Evidences of infection are unmistakable; healing usually occurs but functions are impaired. Sometimes healing is prevented by interference with collapse of abscesses even though defense and repair are potent. Such lesions are to be distinguished from lesions that progress because defense and repair are impotent by means subsequently mentioned.

Ineffective defense and repair fail to suppress bacilli; lesions slowly or rapidly progressive, manifestations of infection, and the outcome are unmistakable.

Resistance, defense and repair fluctuate throughout the course of the disease more or less equally.

All the contributions of local and systemic responses to antagonism are significant but those of the blood are the most effective.

Local responses of the same structures in different persons are equally effective unless there has been previous injury.

The efficacy of systemic responses is dependent principally on the stamina of the units that form blood corpuscles and plasma.

Here again the contributions of all the hematopoietic units to antagonism are significant but those of the plasma (antibodies) are most effective.

As the blood-forming cells weaken, the greater the susceptibility of the host and the less the chances of recovery. This is revealed by repeated blood counts and estimations of sedimentation rates which are found to fluctuate with the course of the disease.

All forms of tuberculosis are systemic infections. All begin with penetration of an external surface, and of these surfaces the mucosa of the digestive tract is the principal offender.

All forms of tuberculosis can be caused by penetration of nutritional surfaces (systemic capillaries) by bacilli deposited on the endothelium from systemic arterial blood although the lymph glands, liver and lungs have other sources of contamination, and the surfaces are open to direct invasion.

The liability of various structures to infection depends on their blood supply, whether they do or do not abstract more than water, salts and food from the blood, on the efficacy of the responses of their parenchymal cells in producing antagonism, and on the stamina of those cells. Proof of the effectiveness and of the peculiarity of the responses of parenchymal cells is found in the susceptibility or insusceptibility of divers structures to human, bovine and avian bacilli.

The myocardium is a dominant factor in combating tuberculosis and is particularly sensitive to the noxious egesta of tubercle bacilli.

PREVENTION

Restriction of the deposition of human, bovine and avian bacilli on external body surfaces would reduce the incidence of the disease materially as proved by eliminating tuberculous cattle from dairy herds. So long as bacilli of the human type are present in the air they will be deposited on bronchial mucosa and the skin and directly or indirectly on ingesta. Bovine bacilli are still present in dairy products. Avian bacilli are contained in the eggs of tuberculous hens which are said to be numerous, and these bacteria are not always destroyed by cooking.

More attention given to personal cleanliness, to the selection, preparation and serving of food, exclusion of the tuberculous from those who handle, prepare and serve food, elimination of tuberculous chickens, prevention of the marketing of milk, butter and cheese of questionable origin and handling are needed to restrict contamination.

This aspect of prophylaxis is not immediately attainable, so that the other aspect, the institution of wholesome methods of living which develop and conserve the stamina of the entire circulatory apparatus, the structures concerned in the formation, rectification and delivery of blood, must be the chief reliance.⁶

Further preventive measures should be more generally employed because it is impossible as yet to determine existing grades of susceptibility or insusceptibility and to estimate how long they may endure. Penetration of the cutaneous surface is infrequent, and of the mucosa of the genito-urinary tract rare, but penetration of the mucosa of the digestive tract not only is frequent but is the common origin of tuberculosis. Bacilli are more likely to penetrate or to be transported in phagocytes through lesions than intact surfaces, and more when contact is prolonged than when it is brief.

Repair and extraction of decayed teeth, the removal of adenoids and of unwholesome tonsils, and the correction of chronic dermatitis are desirable even though glandular tuberculosis has all but disappeared. If it be recalled that bacilli of the human type are not only ubiquitous but are frequent invaders which can be disseminated through the blood or through the lymph without provoking tuberculous lymphadenitis and later reach the blood, then the wisdom of eradicating portals of entry from external surfaces becomes indisputable. By the same token, correction of constipation in persons of the phthisical habitus is necessary, sometimes even when this demands resection of inert intestinal segments.⁷ The indications are as obvious as they are disregarded. First, to eliminate anorexia resulting from indigestion due to stasis; second, to eliminate the toxemia of constipation and thus to improve nutrition; and third, to reduce the frequency of penetration by bacteria of the mucosa and lymph follicles in the affected loops (often terminal ileum and proximal colon), and to obviate the formation of superficial mucous

6. Grades of insusceptibility are commensurate with the strength and endurance of the circulatory apparatus, particularly with the stamina of the blood-forming units, and more especially the lymphoblasts and reticulo-endothelium. The grades of susceptibility are proportionate to the frailties in these structures. There is no distinct demarcation. Lesser grades merge in a common zone wherein there is at one time a modicum of insusceptibility, and at other times, of susceptibility. Higher grades of insusceptibility endure throughout life, however it be prolonged. Lesser grades are dissipated by accidents, disease, unwholesome living and senility. Higher grades of susceptibility can be reduced by proper living but cannot be overcome. Persons so handicapped are destined to die of tuberculosis unless they succumb to another ailment. Their reproduction should be discouraged because inherent frailties are irremediable. Lesser grades of susceptibility can be curtailed, even replaced by insusceptibility, if living is well ordered, and accidents and diseases are escaped.

7. Yates, Raine and Stevens: *Am. Surg.* 90:517, 1929.

ulcers by the prolonged pressure of intestinal contents which favor bacterial invasion.

Summary.—The first and most important step in prevention of tuberculosis is to eliminate human, bovine and avian tubercle bacilli from ingesta. The means are to prevent human bacilli from getting into the air, to stop the sale of milk, butter and cheese containing or likely to contain bovine or human bacilli, and to destroy tuberculous chickens. The second and next most important step is to introduce wholesome living more generally. The third is to minimize the likelihood of penetration of body surfaces by bacilli, more particularly the teeth, tonsils, mucosa and lymph follicles of the digestive tract.

TREATMENT

Treatment consists in assisting patients to develop and to maintain the antagonism that confers insusceptibility, or, if that is impossible, to acquire the least grade of susceptibility. Prerequisite to treatment is a recognition of the existence, the location and progress of the disease and a determination of the existing powers to make and to deliver blood.⁸ Diagnosis and prognosis establish what means, if any, should be employed to augment the defensive capacity of the host, to reduce the offensive power of the bacilli, to conserve the energies of the host and to obviate recrudescences.

Reducing Offense.—Search will sometimes reveal the portal of entry, usually other possible portals, and, when feasible, all should be eradicated because of the probability of reinfection. Should the regional lymph glands contain the predominant lesions or serious lesions that assure dissemination, their radical extirpation is indicated if it can be tolerated. Predominant lesions, wherever located, are harmful because of the local destruction and the dissemination of noxious products and bacilli. Dissemination can be restricted by curtailing the activities of the affected structure. During acute phases complete immobilization is necessary although it induces the atrophy of nonuse in tissue cells, reduces the amount of blood delivered, and thus minimizes antagonism.

8. Deficiencies in the blood develop before tuberculosis can be established. Consequently all persons suffering from tuberculosis, save those well advanced toward recovery, have blood deficits. It is impossible in the earlier phases of the disease to determine promptly which patients have a circulatory apparatus of so little stamina that they will become cachectic despite assistance and therefore cannot recover. Patients seen in the later phases have or have not lost the stamina of their circulatory apparatus. One examination of their blood will not be decisive. Blood counts and estimations of sedimentation rates repeated at intervals while patients are being given appropriate care will demonstrate which have lost hematopoietic capacity and with it the chance to recover. Prolongation of the lives of those hopelessly ill is usually cruel.

As soon as safety permits, gradually increasing activation is indicated, as it assures the utmost recovery of function. If the structure can be sacrificed without jeopardizing life or imposing undue permanent disability (fallopian tubes, testes, ribs, sternum, fingers, toes, etc.) or if such sacrifice is or becomes requisite to recovery (kidney, segments of intestine, extremities, etc.), prompt removal is wisest. Sometimes the predominant lesion demands intervention because of its collateral effect (pressure on the cord by pachymeningitis incidental to spinal caries) and sometimes a subsidiary lesion must be removed (amputation of tuberculous extremities) to permit healing of a predominant lesion (lungs). The proper treatment of abscesses may be perplexing, i. e., whether to aspirate, to institute drainage or to do nothing.

It is easy to recognize the need for operations when they have become imperative and may then be futile. The difficulties are to interpret early indications and to have the courage to act on them or to persuade patients to consent. Estimating the capacity of patients to make blood furnishes more dependable information than any other single factor, though all must be considered, especially the patient's morale.

Augmenting Antagomism.—The first requirement is to improve the quality of blood in circulation, and, if necessary, to restore its volume; the second is to increase the quantity delivered to lesions. Rest is essential, but it can be overdone as well as underdone. Air is not so fresh indoors as outdoors. Ample protection against cold is needed to limit heat production. Patients so protected should be kept on porches most of the time, day and night. Sunshine increases basal metabolism. It stimulates blood production if exposures are restricted to individual needs. Overexposures are more harmful than none. They cause fatigue, curtail the production of both cellular and noncellular elements of the blood, and may suffice to introduce an exacerbation. The benefits of the various artificial lights are greater if the lights imitate sunshine rather than produce part of the spectrum and if exposures are suitably regulated. Diets should provide fuel enough to satisfy current expenditures of energy and to provide for the storage of potential energy but not to overfatten. The requirements in water, salts, vitamins and foods are simple and should be met. Too little water is taken. Provision of salts, particularly iodine, is insufficient. Food-stuffs, perhaps of good quality, are ruined by poor preparation and unattractive service. The tendency to overeating or overfeeding is general. Excess fat is a liability. The digestive tract, often the site of primary invasion and constantly liable to infection, should not be overworked any more than heart muscle. Constipation is a menace.

Blood deficits that are serious when treatment begins or that do not disappear thereafter indicate that blood-forming structures are fatigued

or exhausted. If fatigued, they can be rested and allowed to recover most certainly by repeated transfusions of unmodified blood. Sometimes sugar and salt should be given intravenously to combat dehydration and malnutrition. Transfusions, dextrose and salt given intravenously are most useful in preparing patients for operation, enabling them to tolerate the stresses and expediting recovery. Giving drugs by mouth is usually futile and occasionally is harmful. If the blood-forming units are exhausted, transfusions may only prolong life for limited intervals.

Helping patients to keep their morale high is a major part of treatment. If they need no active measures, they usually know it. If they are in need of more than pacifistic measures, there should be no delay. If they are irremediably affected, telling the truth is sometimes better than continued deception. Amusement, recreation and occupation are as necessary for the mind as suitable diets are for the body.

Exercise is needed to increase delivery of blood, to develop and maintain the robustness of cells and to prevent deterioration. Mental and physical exercise is particularly indicated in combating chronic systemic diseases like tuberculosis.

Conservation of Energy.—The conservation of energy consists not only in restricting the expenditures of energy within limits of necessity but also in promoting the storage of reserve energy to provide a margin of safety. The hypermetabolism that produces fever necessitates compensatory rest. Lower grades of fever permit of some exertion. Afebrile states indicate exercise, gradually increased, but always within the limits of undue fatigue. Thus alone may the warehouses that store sources of reserve energy be enlarged and filled. Undue caution in reactivation prolongs convalescence and sometimes induces incapacitating temerity or permanent inertia.

Prevention of Recrudescences or Recurrences.—Development of the disease proves deficient antagonism. However complete the apparent immediate recovery, some of the bacilli inactivated to transient saprophytism probably persist in the body, and, even if they do not, reinvasion is certain. It is impossible to differentiate temporarily increased resistance from permanent immunity. It is safest to assume that the immediate insusceptibility is low and likely to be dissipated, possibly years hence. Wholesome living, a suitable occupation, and the avoidance of exposure to reinfection should be continued throughout life.

PULMONARY TUBERCULOSIS

Lungs are remarkably resistant to invading bacteria; their defensive capacity is exceptionally high, and, when unhandicapped, they are able to effect well-nigh scarless healing of fairly large lesions. The causes

of their being so commonly involved in all tuberculous processes and the measures that will promote recovery from pulmonary tuberculosis are revealed in the peculiarities of their structure and function.

The significant structural characteristic is the unique disproportion between the vast total expanse of the five lung surfaces and the limited bulk of parenchyma. The external or ventilating surface is formed by the bronchial mucosa and the cells lining the 404,000,000 alveoli. Aebly has estimated the area of the alveolar cells in an adult at the end of inspiration to be 79 square meters during intervals of rest and 129 square meters when activities are highest. This is about 40 to 70 times the average skin surface (1.8 square meters) without considering the expanse of bronchial mucosa and is from 75 to 125 times as large as the surface of the intestinal mucosa (1 square meter?). The internal or aerating surface, formed by the endothelium of the capillaries of the lesser circuit, approximately equals the external surface during inspiration and expiration, whether quiet or labored. Mesothelium forms the pleural surface, lymphatic endothelium the drainage surface, and hemangio-endothelium of the capillaries of the greater circuit the nutritional surface. The bronchial vessels are under systemic vasomotor control, which is absent in the pulmonary vessels. Lying beneath, on and between the pulmonary surfaces and surrounding the blood and lymph vessels is the restricted parenchyma which is both supporting and contractile.

The functions of the lung are external respiration, filtration of inspired air, filtration of blood delivered through the pulmonary arteries, elaboration of antibodies and digestion of fats and carbohydrates.

External respiration or aeration of blood is requisite not only to survival but to activity. Moderate impairment of its effectiveness restricts the production of functions needed for exertion and to combat disease. Immoderate impairment limits the production of functions to those required to support inactive life or reduces them below the limits of viability.

Aeration continues if a balance is maintained between the volume of continuously ventilated alveolar air and the volume of blood driven at normal velocity through the capillaries of the pulmonary circuit. Either of these factors may vary widely and abruptly under usual conditions, yet, because of the automatic action of the air-cell-capillary mechanism discovered by Dunham, their coordination is assured provided the heart remains competent and the lung retains its elasticity. The mechanism is as promptly effective under unusual conditions. The interrelationships that obtain in human beings are easily summarized.

If air is prevented from reaching alveoli by obstruction of a bronchus, there is almost immediate atelectasis, and a corresponding

collapse of the pulmonary capillaries. The blood normally destined to flow through the collapsed vessels is diverted to adjacent unaffected capillaries which are overfilled. This causes a compensatory emphysema, and the excess blood is thereby aerated. Should a branch of the pulmonary artery be occluded, the capillaries distal to the occlusion collapse, and atelectasis is a prompt consequence. Again blood is diverted, produces a compensatory emphysema and assures aeration. Other abnormal states produce similar adjustments. Consequences are similar if an entire lung is affected. Reduction in intrapleural negative pressures which produce successively deflation and collapse or a production of positive pressures that impose compression of the homolateral lung causes diversion of blood to the other lung and compensatory emphysema within it.

Prompt and proportionate responses to usual and unusual influences which produce the extraordinary adaptability of the lung likewise make it vulnerable. Atelectasis following deprivation of air or of blood from the pulmonary artery, if prolonged, becomes permanent because of the contractility of the parenchyma, vessels and bronchi. Similarly, protracted collapse and compression which check respiratory movements prevent recovery of elasticity. Deflation on the contrary permits some respiratory movements, preserves pulmonary elasticity, and full inflation occurs when normal intrapleural negative pressures are reestablished. Interruption of the flow of blood through the bronchial arteries which are end-vessels causes necrosis of the lung structure affected, including its overlying pleura. Blood in the bronchial arteries supplies not only nutrition to the entire lung but also the cellular and noncellular elements that contribute the major part of resistance, defense and repair.

The effects of parenchymal lesions which restrict blood, lymph and air conduction or impair elasticity are similar to reductions in the volume of blood in circulation, in its oxygen-carrying power or in its pressures because of myocardial subcompetence. All interference with external respiration and the extent of the interference is commensurate with reductions in vital capacity and breath-holding time.

Filtration of the inspired air removes foreign bodies and noxious gases. Dust and bacteria, some of them pathogenic, are present in the air. The amount of dust and the number of bacteria inhaled are far larger than are exhaled, the balance being deposited on the walls of air passages. The amount of dust and the number of bacteria deposited within the lung diminish with the distance from the origin of bronchi. If the mucosa is intact and the passage of air is unobstructed, the ultimate bronchioles and alveoli are uncontaminated. Abstraction of irritating gases from air is less effective. The chief defense is limiting inspiration and promoting expulsion.

Filtration of blood includes the removal of foreign bodies (inert particles, bacteria and dead or dying cells) and the abstraction of noxious products. This form of physical and chemical filtration of the lymph is effected by lymph glands, of the portal blood by the liver and of the arterial blood in the systemic circulation to some extent by all structures, including the lungs, but mainly by kidneys, spleen, liver and the intestinal tract. All noxious products and foreign bodies in the systemic arterial blood, in the portal blood and in the lymph that escape the filtration just outlined and all that enter the systemic venous blood are delivered to the lungs in the blood in the pulmonary arteries unless there is a patent foramen ovale. Lymph from the receptaculum chyli is the chief source of bacterial contamination, particularly during periods of active intestinal digestion when some bacteria are present and a part of them are pathogenic. Abstraction of noxious substances from the blood by the aerating surface is prompt if they are volatile (alcohol, ether, acetone, etc.) and probably also if they are not. The efficacy of the external and aerating surfaces of the lung as filters of foreign bodies is proved by pneumoconiosis, the black spit of those inhaling coal dust, the failure of insufflation to drive bacteria into bronchioles and alveoli, the common presence of bacteria in the lymph and the relative infrequency of bacteria in the arterial blood as compared with venous blood in the systemic circulation.

Fried⁹ indicated at the last meeting of this association that antibodies were produced by the endothelium of the pulmonary capillaries, the cells lining the alveoli and certain cells within the parenchyma, also that these cells could digest fats and carbohydrates.

INCEPTION

The first requirement is penetration of one of the five surfaces of the lung by tubercle bacilli. The second is that the bacilli shall invade the parenchyma, and the third that the antagonism offered by the host shall be insufficient to inactivate or to destroy the invaders by restricting the rates of their metabolism to viable limits or by reducing the rates below those limits. The surfaces will be considered separately.

External Surface.—Inert foreign bodies, bacteria and probably tubercle bacilli¹⁰ are constantly present on the mucosa of bronchi and larger bronchioles that have submucosa, rarely, if ever, under normal conditions on the surface of the ultimate bronchioles and the alveoli which have none. Penetration of bronchial mucous membrane by bacteria occurs as has already been described for other surfaces. Bacilli, under pressure exerted by secretions or exudates, pass into, through or

9. Fried, B. M.: Defensive and Metabolic Apparatus of Lungs; Lungs and Macrophage System, *Arch. Path.* 6:1008 (Dec.) 1928.

10. Opie: *Am. Rev. Tuberc.* 14:347, 1926.

between cells of an intact mucosa, through lesions of the mucosa or are transported within wandering phagocytes.¹¹

A portion are retained in the mucosa or submucosa. Those able to maintain parasitic activities provoke lesions (bronchitis and peribronchitis); the balance are inactivated to saprophytism or are destroyed. The other portion of the invaders penetrate the walls of capillaries or are carried through them in phagocytes and are transported in the blood of the bronchial vein or in the lymph.

Bacilli transported in the blood in the bronchial veins are returned in the blood in the pulmonary artery. Those transported in the lymph pass to the peribronchial glands in which the majority are removed. According as they are active or are inactivated they do or do not cause tuberculous lymphadenitis. Lymphadenitis does or does not obstruct the intraglandular sinuses and does or does not result in destruction of the gland capsule with production of active periadenitis. If the intraglandular sinuses are obstructed, the lymph is compelled to flow through collateral channels, some of which pass through lymph follicles within the parenchyma of the lung. Thus bacilli are deposited in the intrapulmonary lymph follicles and the consequences are the same as if they are deposited in peribronchial lymph glands. If folliculitis develops, it may progress to an active tuberculous perifolliculitis.

Periadenitis and perifolliculitis, tuberculous bronchitis and peribronchitis may result in pulmonary tuberculosis by direct extension. Otherwise there is little likelihood that the parenchyma of the lung will become directly involved from penetration of its external surface. Indirect parenchymatous involvement by bacilli transported in the lymph is probably infrequent at onset, whereas this form of involvement by bacilli transported in the blood in the pulmonary artery is common.

Available evidence indicates that virulent tubercle bacilli are commonly, if not constantly, present on the bronchial mucosa proximal to the ultimate bronchioles and that this portion of the external surface of the lung is repeatedly penetrated by the bacilli. After penetration

11. The black spit of those breathing air containing coal dust proves that foreign bodies are expelled with bronchial secretions. Tubercle bacilli are seldom found in the sputum of persons who have not active pulmonary tuberculosis, and not always when they have the disease. Pneumoconiosis proves that not all foreign bodies present on the external surface are expelled with secretions, and the lesions suggest that the lymphatics are active in removing such as pass through this surface. Insufflation of bacteria into bronchi does not carry them to the ultimate bronchioles and alveoli. Causing susceptible animals to breathe air containing tubercle bacilli does not invariably provoke pulmonary tuberculosis, but this is almost a constant consequence of intravenous injections thereof. Presumably the number of tubercle bacilli present on the external surface of the lung is not large enough to be expelled as is coal dust, and their presence is not of necessity a menace.

the majority of the invading bacilli enter or are carried into the lymphatics. Though they frequently cause peribronchial tuberculous lymphadenitis and perhaps intrapulmonary tuberculous lymph folliculitis, these lesions are infrequently the origin of parenchymal lesions. On the other hand, the minority of the invaders carried in the blood in the bronchial veins are returned to the lung within the pulmonary artery and are often the cause of the disease.

Aerating Surface.—The number of bacilli that penetrate the external surfaces of the body at one time is small, but this occurs so often that the aggregate is large. A proportion of the invaders eventually are transported in the blood in the pulmonary artery and the majority of them are deposited on the aerating surface, relatively few passing on to be disseminated in the arterial blood of the systemic circuit. The bacilli present on and within the endothelial cells of the pulmonary capillaries, perhaps those within phagocytes in the parenchyma, explain in part why Opie found virulent organisms in bits of lung wherever they were excised.

Penetration of the aerating surface by organisms deposited on it is the most certain origin of pulmonary tuberculosis and the commonest. The sources of the bacilli are from penetration of an external surface of the body and from extrapulmonary tuberculous lesions. Penetration of skin and of the mucosa of the genito-urinary tract is infrequent; of the external surface of the lung is repeated, and of the mucosa of the digestive tract is frequently repeated. These facts explain why digestive disturbances frequently occur at or before the onset of pulmonary tuberculosis and why pulmonary and extrapulmonary lesions are often coexistent.

Nutritional Surface.—Bacilli must be present in the blood in the bronchial artery if pulmonary phthisis is to arise from invasion subsequent to penetration of the nutritional surface. In order to gain the systemic arterial blood, bacteria must pass through the pulmonary circuit unless there is an open foramen ovale. The majority of organisms are deposited from the blood in the pulmonary artery on the aerating surface, so that the inception of pulmonary tuberculosis from bacilli deposited on the nutritional surface is exceptional save in generalized military tuberculosis.

Bacilli are disseminated in the systemic arterial blood and sometimes without provoking pulmonary lesions; for example, to the bones and to the central nervous system. It is important to recall that in pulmonary tuberculosis, even in its incipency, bacilli are disseminated through the systemic arterial blood and do cause extrapulmonary lesions, notably renal.¹²

12. Medlar: *Am. J. Path.* 2:401, 1926.

Drainage Surface.—The drainage surface is large in proportion to the bulk of the parenchyma. Lymph flows from the periphery toward the hilum in the peribronchial and parenchymal vessels which intercommunicate and is delivered into the afferent sinuses of the tracheal glands. Lymph gland units are placed at intervals along the lymph vessels. The consequence of removal of bacilli from the lymph stream has already been outlined in the discussion of invasion through the external surface. One other detail is noteworthy. If the sinuses within a tracheal gland become obstructed by tuberculous adenitis, the outflow of lymph through these channels is prevented. Lymph then flows from the hilum toward the periphery until it finds egress through unobstructed afferent channels. In this way there may be a retrograde infection of glands, a subsequent periadenitis with extension to the parenchyma. Seldom would this occur in the establishment of a primary pulmonary lesion.

Atypical lymph vessels develop in adhesions between visceral and parietal pleurae. Thus the glands in the inferior cervical region are commonly involved if there are apical lesions and adhesions. Contrarily, tuberculosis of the cervical glands might extend thus to involve the lung.

Pleural Surface.—The initial intrathoracic tuberculous lesion might be in the pleura caused by bacilli delivered through the bronchial artery or deposited on the visceral pleura from lesions in the thoracic cage or adjacent glands. The usual sequence is extension from a subpleural parenchymatous focus.

Summary.—Pulmonary tuberculosis develops only in susceptible hosts after penetration of one of the five surfaces of the lung by bacilli that had entered the body through one of its external surfaces that may or may not have produced extrathoracic lesions.

Pulmonary tuberculosis is the common form of the disease or the common concomitant of other forms not because the parenchyma is unable, if normal, to contribute affectively to antagonism but because bacilli are deposited at brief intervals on its aerating surface, and the lung is subject to repeated injuries that vitiate its responses to subsequent irritations.

The chief sources of bacilli are penetration of the gastro-intestinal mucosa and of the bronchial mucosa proximal to the ultimate bronchioles, and extrathoracic foci of tuberculosis.

The chief avenue of infection is penetration of the aerating surface by bacilli deposited on it from the blood in the pulmonary artery.

EVOLUTION

After the inception of lesions in the lung, which occurs only in susceptible hosts, their subsequent evolution is quite the same as in other structures, and the course varies with the existing degree of suscepti-

bility. The natural contributions of the activities of its component cells to resistance, defense and repair are uncommonly effective, the blood supply is large, and the lung is highly adaptable. On the other hand, lungs are very sensitive to alterations in tension, even to the slight changes caused by incipient lesions because the volume of parenchyma is so restricted. Direct and indirect consequences of the alterations are reductions in the amount of blood delivered through branches of the bronchial artery which furnishes most of the nutrition and contributes mainly to antagonism.

Lesions in least susceptible hosts seldom exceed miliary tubercles, and were they not frequently calcified would be undetectable. They do not impair function. Recovery of these patients cannot be prevented by maltreatment, but it can be expedited by favorable treatment. As the lesions develop in moderately susceptible hosts they create increasing tension which interferes with the passage of air, compresses the pulmonary capillaries and terminates in atelectasis in the portion affected. Atelectasis reduces the supply of bronchial arterial blood. Atelectasis also promotes fibrosis, and this is hastened by the inflammation. Fibrosis is favorable to healing but unfavorable to resistance and defense because the systemic blood supply is curtailed. Unless the bacilli are promptly inactivated, a vicious cycle is inaugurated. Interference with the delivery of blood permits lesions to extend, and the larger the lesion, the more the restriction of blood supply and the greater the liability to caseation. A majority of these patients will recover if given only proper expectant care, but the duration of their illness and the extent of their lesions is avoidably great. Some who develop larger cavities because of untoward local conditions will only recover or be enabled to arrest the progress of their disease if intrathoracic tensions are so altered by operations as to assure collapse of the cavities.

Lesions develop in immoderately susceptible hosts in three ways: 1. When the offense-defense ratio is low, the irritation is slight and the responses are sluggish. A gradually progressing fibrosis results which cannot be materially controlled. 2. When the offense-defense ratio is high, lesions develop and extend more rapidly, caseation is pronounced and multiple cavities are formed. Drainage is inadequate, toxemia is higher and more bacilli are disseminated. The lives of a few of these patients can be prolonged if their cavities are collapsed, and some can be made more comfortable. The majority are too ill to withstand operation, or, if they survive, are unable to effect enough repair to justify the discomforts and danger. 3. When the offense-defense ratio is very high, acute pneumonic phthisis develops and is seldom amenable to treatment.

Invaluable clinical lessons can be learned from the progress of lesions in the lung. At onset all lesions are incipient, and, excluding the pneu-

monic processes, it may be impossible promptly to differentiate grades of susceptibility. Safety demands that each patient be regarded as less competent to develop antagonism than observations may indicate. Whatever measures will promote recovery without imposing undue handicaps (e.g., permanent reduction in vital capacity) should be utilized at once, not after waiting to observe progress. Similarly when patients are seen after onset, the measures that will retard progress without adding materially to handicaps should be employed before the possibility of recovery or even of arrest is forfeited provided that has not already been lost.

The stresses imposed by the disease affect the whole body, more particularly the circulatory apparatus. Blood formation, originally inadequate, is apt to be further impaired by fatigue and intoxication of all hematopoietic structures, especially the weaker units, the very ones that because of their incompetence the disease was established. Heart muscle is similarly affected and myocardial weakness is often more serious than the pulmonary lesions. Vital capacity is reduced and restricts the production of the excess energy required to provide defense.

Every new lesion in the lung or pleura reduces the elaboration of antibodies, increases dissemination of noxious substances and bacilli even more than the inception and progress of other lesions. The greater the number of bacilli disseminated, the more certain the development of multiple extrapulmonary lesions. All foci of pulmonary disease raise peripheral intravascular resistance which increases cardiac burdens. In brief, the earlier the disease, the more hopeful the outlook, and the more inexcusable is procrastination in employing aggressive therapy.

Summary.—Evolution of pulmonary tuberculosis is determined by the nature and extent of the deficits in constituents of the blood, whether the deficits result from fatigue or exhaustion of the structures that form those constituents, and by alterations in intraparenchymal tension.

When the disease is in its incipency, it is seldom possible to determine at once the capacities of patients to develop the antagonism needed for recovery or to arrest progress.

Safety demands that each patient be regarded as less than apparently competent and be treated as promptly and as aggressively as conditions warrant.

None would be injured if this plan were followed. The recovery of those of least susceptibility would be expedited, and of those of moderate susceptibility would be assured with the least immediate and ultimate disability. The lives of those of immoderate susceptibility would be prolonged.

When the disease is moderately advanced, it is usually possible to determine within a few weeks, as will be described later, whether or not recovery or arrest is attainable by some form of active intervention. If

the disease is immoderately advanced, the objectives are to prolong active lives and to restrict discomfort, not to protract existence.

PREVENTION AND TREATMENT

Prevention.—The chief sources of contamination are bacilli in air and ingesta. The more serious portals of entry are in the mucosa of intestines, bronchi and larger bronchioles, tonsils and carious teeth.

At present the number of bacilli in air and ingesta cannot be reduced although the means are obvious. Affected tonsils can be removed and carious teeth corrected. Wholesome living will afford all possible protection against bronchial and intestinal lesions. Some persons are unfortunate heirs to weak intestinal muscles which are often more pronounced in the proximal and terminal segments of the colon. Weakness causes stasis, digestive distresses and malnutrition. Stasis favors penetration of the intestinal mucosa by bacteria and absorption of noxious substances. Malnutrition vitiates antagonism. If constipation cannot be otherwise relieved, operations are sometimes indicated. Justification for care in correcting gastro-intestinal malfunctions, even though it entails serious operations, is found in the frequency of digestive disturbances preceding inception of pulmonary lesions, in the common development of intestinal tuberculosis in those suffering from pulmonary phthisis and in the knowledge that a large number, if not the majority, of tuberculous infections of the lungs are caused by bacilli that invaded the intestinal mucosa. Suitable hygiene will always be the effective means to conserve and to augment insusceptibility and to reduce the grades of susceptibility.

Treatment.—Pulmonary tuberculosis is a systemic infection with tubercle bacilli wherein the predominant lesions are in the lungs. It begins because the responses of tissue cells adjacent to invading bacilli are supplemented inadequately by the cellular and noncellular constituents of the blood delivered through the bronchial artery. Although the efficacy of tissue cell responses may be impaired through previous injury, deficits in some of the constituents of the blood are the constant and determining contributing factor in the origin and throughout the progress of the disease. Recovery occurs spontaneously if the structures which produced the constituents initially deficient are sufficiently robust to respond to the added stress of toxemia by overproducing instead of underproducing those constituents, if the lesions in the lung receive abundant blood and if they have not progressed beyond repair. Recovery can be promoted if therapeutic agencies minimize or eliminate the obstacles to spontaneous recovery.

Treatment consists primarily in improving the quality of blood in circulation and restoring its volume if it has been reduced but not because

of the lungs alone. Lesions, be it recalled, are never restricted to the lungs. Either an extrapulmonary focus was the source of the infection that has reached the lungs or bacilli from the pulmonary lesion have been disseminated chiefly through the systemic arterial blood and deposited on the nutritional surface of organs and tissues. The majority are destroyed. Some are inactivated. A few remain parasitic and produce lesions, possibly in the kidneys (*Medlar*). *Other steps in treatment* are to restrict further dissemination of bacilli and of noxious substances from the pulmonary foci, to increase the volume of blood delivered to the affected or more affected lung, thus to foster the efficacy of the defensive and reparative responses of its structural cells, to conserve myocardial competence and to develop and maintain a margin of safety which includes upholding morale.

Improvement in the Quality and Restoration of the Quantity of Blood in Circulation.—The need for well balanced diets, suitably prepared and served, is recognized but infrequently met. The sin of overfeeding is as common as is the neglect to utilize proper food to regulate the bowels. Constipation is a double menace, interfering with nutrition and favoring invasion or more often reinvasion of intestinal mucosa by bacilli swallowed with the sputum. Seldom do patients get enough water, fresh fruit and salads. Calcium, iodine and chlorine are insufficiently provided. Fresh air and sunshine, two necessities everywhere available, are seldom properly utilized. Outdoor living, night and day, requires sleeping porches and extra attention. This increases immediate costs but saves eventually. Perhaps one tenth of the patients are too ill to benefit from regulated exposures to sunshine. Certainly not one-tenth are allowed to profit from the beneficent influence that energizes the metabolism of all cells.¹³

13. Facts are available to contradict the harmful statements of those opposed to the therapeutic utilization of sunshine. Persons (excepting negroes) having moderate deficits in either cellular or noncellular blood elements who are otherwise living wholesomely will recover from their anemia if exposures to sunshine are properly regulated as suggested by Rollier, provided their hematopoietic structures are not exhausted. On the contrary, robust persons overexposed even once to real or artificial sunshine will develop deficits in both cellular and plasma constituents (e. g., lymphopenia and hastened sedimentation) that may persist for more than a fortnight. It is therefore evident that exposure of those suffering from moderate fatigue of hematopoietic structures must be initially brief and gradually increased, and those whose blood-forming units are exhausted will be injured by any exposure.

Both the beneficial and injurious effects are produced by emanations that penetrate the skin and are disseminated in blood and lymph. Sunburns and tan are reactions to overexposures and are to be avoided in therapy—burns because they are indicative of injury, tanning because it is protective against the penetration of the skin by emanations and necessitates longer exposures to provide desirable benefits and leads to additional pigmentation. Hence the wisdom of gradually

Artificial light which reproduces the entire spectrum of sunshine quite accurately can be furnished and is a satisfactory substitute, but only a substitute. Artificial lights that produce parts of the spectrum are less efficacious. Drugs avail little. Intravenous administration of dextrose and salt is valuable to overcome dehydration and alkalosis. When repeated examinations of the blood show that blood formation continues to be subnormal under this regimen or that blood deficits are serious at the beginning of treatment, transfusions, often multiple but of unmodified blood, are indicated unless patients are irreparably involved.

Restriction of Dissemination of Noxious Products and Bacilli.—Limitation of excursions of both lungs is attainable by mental and physical rest. A further restriction but not abolition of excursions of the affected or more affected lung is quite imperative. It can be provided by reducing the intrapleural negative pressures on that side either by artificial pneumothorax or preferably by induced paralysis of the diaphragm.

Fostering Defense and Reparative Responses of Tissue Cells.—Restriction but not abolition of usual activities and hyperemia are required. Means to restrict motion and the amount of blood needing aeration and filtration have just been described; those to increase the blood supply follow. Sometimes cavities must be allowed or compelled to collapse by the further reduction or abolition of intrapleural negative pressures. Induced pneumothorax may be utilized. Partial or complete thoracoplasty is usually demanded.

Increase of Amount of Blood Delivered to Lung.—Parenchymal nourishment and defense are supplied chiefly by the blood delivered through the bronchial arteries which are under vasomotor control. The unit volumes of blood delivered are greatest if the peripheral resistance is minimized and vasoconstriction prevented. Peripheral resistance is least when the lung is in a mean position between the extreme of inflation and deflation. Vasoconstriction is caused by chilling of the body and complete inactivation of the lung. Keeping the body warm and reducing intrapleural negative pressures fill these requirements. Increased metabolism of tissue cells adjacent to bacilli produces the excess catabolic products needed to induce local hyperemia.

Conservation of Myocardial Competence.—Restriction of toxemia, adequate nourishment, rest in bed during the active phases of the disease, and thereafter gradually progressing activation are required. Most

exposing increasing areas of skin so that maximal effects are attainable in brief intervals. Likewise it is inexpedient to expose to sunshine during midday in the summer or to highly powerful artificial lights. The notions that the thoraces of patients suffering from pulmonary tuberculosis should not be exposed and that any exposures provoke hemorrhage are obviously erroneous.

important of all is the provision of an adequate volume of wholesome blood, and second to this, the limitation of the peripheral resistance within the vessels of the lung, which is attainable by the avoidance of positive intrapleural pressures.

Margin of Safety.—A supply of reserve energy during the disease is hardly more necessary than it is throughout life after convalescence. If the capacity of the entire circulatory unit to make and to deliver blood is developed and not dissipated, the utmost has been accomplished.

Morale.—The will to recover and to keep well is aggressive optimism. Optimism is developed and maintained with the realization that suitable efforts are being made to promote mental as well as physical welfare. Gaining in strength alone is of little value without a desire to work and an anticipation of the reward of accomplishment. Nothing is more productive of, pacifistic pessimism than the expectant therapy that procrastinates until body and soul are wrecked.

SURGICAL ASPECTS

Operations suitably performed on properly selected patients are efficacious in promoting recoveries or in aiding to arrest the disease. Failures have taught the invaluable lessons of what not to do and when not to do anything. Successes indicate greater service, particularly to many who are being denied a more certain and less delayed return to active life. A summary of experiences gained while attempting to promote recoveries by a utilization of procedures based on concepts of the pathology of tuberculosis and of the physiology of external respiration will be given to indicate possible attainments.

TRANSFUSIONS

Unmodified blood has been given with paraffined tubes.¹⁴ Many patients have received one, some three or four, and a few seven or more transfusions.

14. Among the objects of transfusion are to increase the volume of blood in circulation, to raise its oxygen-carrying capacity, to add both lymphocytes and protective substances or antibodies, and to avoid causing febrile reactions.

Anticoagulants now available are injurious to lymphocytes and to antibodies. Margaret Perry (Wisconsin M. J. 25:123, 1926) found lithium citrate to be the least harmful. All of the fibrinogen is not inactivated and is changed into substances that approach fibrin in structure. These substances are sufficiently irritating to cause chills, particularly in the febrile patient, whose thermo-regulating apparatus is unstable. Chills are distinctly more injurious than helpful and may be lethal. Syringes are not used for the same reason. They injure blood more than do paraffined tubes and thus initiate the conversion of fibrinogen into fibrin. Chills occur less frequently after syringes are used than after anticoagulants are employed but more frequently than when transfusions are given with Vincent tubes.

Indications.—Serious blood deficits, preparation for operation, post-operative hypotension, and incipient acute pneumonia especially in the less affected lung are indications for transfusion.

Contraindications.—Transfusion is contraindicated in the presence of irrecoverable incompetence in the blood-forming structures or in the heart muscle.

Failures.—Once the capacity to form cellular or noncellular constituents of the blood is lost or the myocardium is irreparably damaged, transfusions, no matter how often repeated, are futile though they may prolong life for a few weeks or even months.

Successes.—Restoration of the quality and quantity of blood has been achieved, and the rest thus provided has permitted the circulatory apparatus to recover its competence. Sometimes when the heart is weak, it has been necessary to give only 100 cc. at a time; usually 500 cc. has been given and as slowly as the avoidance of coagulation permitted. Patients have been prepared to withstand operations that would otherwise have been exceedingly hazardous. Similarly they have been relieved of ominous postoperative hypotension. Rarely a transfusion has been given during operation, though usually dextrose is given if blood pressures fall below safe limits. Transfusions given as soon as signs of an acute pneumonia are recognized can, because of the resultant overdilatation of the pulmonary capillaries, overcome atelectasis, and promote immediate recovery from the infection.

The interdependence of lesions and blood status has been proved. Nothing added to the routine treatment of patients but the giving of blood has induced improvement that cannot be otherwise interpreted. Another proof was obtained accidentally. A large man who had recovered from a rather brisk form of the disease had been used as a donor for a very sick patient, and his blood was more beneficial than that of the usual donors. Shortly afterward a nurse became acutely ill and needed blood immediately. He volunteered to give his blood, and this additional reduction was followed by a recrudescence which, fortunately, was brief. When doubt arises, it is safer to transfuse than to wait for positive indications. One transfusion too many never hurt a patient; many fail to obtain full benefits if there is one too few.

The selection of donors is also of importance. Those recently recovered from the disease are seldom available and, as experience proves, should be used only under unusual conditions. Robust persons over 30 years of age and more particularly men who have had tuberculosis and acquired insusceptibility are most suitable. They have potent antibodies in their plasma, the substances which restrict the metabolism of bacilli, help to neutralize the noxious products and contribute the most effective single element to antagonism.

INDUCED PARALYSIS OF THE DIAPHRAGM

Paralysis and subsequent rise of the diaphragm reduces intrapleural negative pressures (in man and other thick-pleuraled animals but not in the thin-pleuraled) and causes deflation of the lung on the side affected. Vital capacity is reduced upward of 10 per cent. In some patients the intercostal spaces are narrowed, and the angle between ribs and spine becomes more acute immediately or some weeks after paralysis. This handicap is not great, but suffices to justify induction of permanent paralysis only when recovery of function of the diaphragm would be impossible after the pulmonary lesions have healed.

Three procedures are employed: crushing (*phrenemphraxis*) of the main branch of the phrenic nerve or, in addition, of such accessory branches as contain filaments that transmit motor impulses to induce temporary paralysis and, if possible, complete relaxation; excision (*phrenisectomy*) of portions of the trunk or accessory branches of the phrenic nerve to induce permanent complete paralysis and relaxation; extraction of the distal portion of the phrenic nerve (*exeresis*) when *phrenisectomy* fails to induce complete paralysis and relaxation.

All operations are performed with patients lying on a fluoroscopic table. The position and contractions of the diaphragm are observed. Then the phrenic nerve is exposed through a supraclavicular transverse incision, the main trunk held gently in a narrow hemostatic forceps, the lights extinguished and the x-rays generated. Sudden crushing causes the diaphragm to contract and then to rise abnormally high. If all the motor fibers have been blocked, the diaphragm does not descend during inspiration, and its contour remains evenly rounded. If some filaments transmitting motor impulses lie in accessory or collateral branches (less than 40 per cent), then on inspiration wavy indentations appear in the contour produced by the unparalyzed segments. Collateral branches are sought and the process repeated until the paralysis is complete; i. e., there is no intrinsic motion though the paralyzed side may be drawn downward by contractions of the opposite side. Branches of sympathetic nerves transmit impulses that help to preserve the tone of the diaphragmatic muscles. They may join the phrenic in its cervical or thoracic portions or reach the diaphragm separately. Until these nerves are blocked, the diaphragm retains some of its tone and is incompletely relaxed. When they are all blocked, relaxation is complete and the atonic diaphragm rises during inspiration, producing the characteristic paradox.

If *phrenemphraxis* as just described produces desired results and it is expedient to make them permanent, the nerves containing motor fibers are divided at the place where they have been crushed, a few inches of the distal portion withdrawn and divided as low as exposure permits.

When the phrenemphraxis is inefficacious, exeresis is utilized. The main trunk is divided and the distal portion extracted slowly until the nerves are disrupted. Even this procedure may fail occasionally to induce relaxation or even complete paralysis.

Indications.—Temporary paralysis is used for incipient lesions and for moderately advanced lesions which are of such nature as to indicate probable healing in four months or less and a return of motion will be helpful in restoring vital capacity, for recurrent hemorrhages from the pulmonary artery and for pain. Permanent paralysis is induced as a preliminary step to thoracoplasty if return of motion is undesirable.

Contraindications.—Immobilization, high position and fixation of the diaphragm by dense adhesions over the lower lobe, immoderate susceptibility revealed in irremediable blood deficits, and approaching death are contraindications for produced paralysis.

Failures.—Occasionally it is impossible to find accessory branches that transmit some of the motor impulses to the diaphragm, and crushing induces only partial paralysis. Not only is motion incompletely inhibited but also the diaphragm retains enough tone to prevent its displacement upward. Rarely exeresis will not induce complete paralysis, some innervation of the diaphragm being supplied by the lowest intercostals.

Paralysis of the diaphragm, however complete, will accomplish little for those of immoderate susceptibility even if their lesions are not advanced. It is only a part of treatment, and, unless accompanied by all other measures, it will often fail to promote improvement. Those who expect induced paralysis to be a panacea are disappointed because they do not rely on careful physical and fluoroscopic examinations, do not consider personal and family history, and neglect to estimate hematopoietic capacity.

Successes.—The greatest help obtainable from transient paralysis is for incipient lesions. Recovery, if patients are of lesser grades of susceptibility, is hastened. Improvement in similar types of patients whose lesions are more advanced is usually pronounced and progressive and may even lead to their dismissal from an institution within four months as apparently recovered. Sometimes a recrudescence then proves that the disease had been arrested with the aid of paralysis and was reactivated by a return of motion. Patients with advanced lesions may be made more comfortable through restriction of pain and cough. Some are helped mentally for a time. A notable service is in preparation for thoracoplasty. Hemorrhages from the pulmonary artery are usually controlled. Pain can sometimes be checked. Occasionally the sensory nerves are in accessory branches so that blocking only the main trunk of the phrenic nerve is useless.

Reduction in intrapleural negative pressures and consequently in the inflation and excursion of the lung increases its blood supply, raises pleuropulmonary resistance to invading bacteria, augments defense and repair, and does not increase cardiac labor. It is a natural adaptation to combat acute pleuropulmonary irritation and is accomplished by spontaneous reflex atonicity of the diaphragm, increased angulation of the ribs and restricted motion of the thoracic cage on the affected side. Induced paralysis of the diaphragm affects the same reflex arcs and is similarly effective. It is not the treatment of tuberculosis but is a dependable adjunct to other methods. The earlier it is employed, the more benefits it will confer if the trifling operation is performed carefully and permanent paralysis is not induced when transient paralysis would suffice.

Pneumothorax, properly induced and repeated, will provide an inconstant reduction in intrapleural negative pressures. It creates a lesion, a cavity filled with an irritating gas. Instead of effecting a natural and dangerless adaptation, it imposes an abnormal state, not without danger, that is less beneficial.

THORACOPLASTY

Extrapleural resection of ribs is not a definite procedure such as an amputation or removal of a gallbladder but a means to alter intrathoracic tension. Alterations attained depend on the number and location of ribs resected, the extent of the resection, the presence or absence of pleural adhesions and the elasticity of the lung.

The utmost accomplishment of complete thoracoplasty is to subject an entire lung to atmospheric pressure and produce its collapse. This permits the lung to adapt itself naturally and to retain a suitable supply of bronchial arterial blood during and after the interval of readjustment without imposing intolerable burdens on the heart if operations are performed in three or more stages. Fortunately, the lung is not compressed, its blood supply is not harmfully curtailed and the heart is not overburdened. Addition of pressure to the parietes after ribs are removed is worse than futile.

Indications.—Existence of cavities that cannot collapse because their walls are too rigid or because they are fixed by pleural adhesions to parietes demands thoracoplasty to provide opportunities for arrest of the disease or recovery from it. Limited thoracoplasty is indicated if the cavitation is restricted to an upper or a lower lobe and the balance of the lung is so little affected that it can recover and contribute to external respiration and other pulmonary functions. Complete thoracoplasty is indicated if cavities exist in more than one lobe or if they are confined to one lobe and the lesions in the balance of the lung suffice to have

destroyed its capacity to regain function; if incomplete, thoracoplasty fails to promote arrest or recovery.

Contraindications.—Loss of blood-forming powers, pronounced and irreparable myocardial incompetence, progressive bilateral lesions and lack of morale are included in the contraindications.

Methods.—Patients are selected who have an opportunity to recover. Rib-cutting will not rehabilitate the dying and is never justified merely because everything else has been tried and has failed. Preparation extends over a week or longer. It consists of a preliminary paralysis of the diaphragm, restricted activities, excess of water and fruit juices in the diet, intravenous administration of salt and dextrose, and, when feasible, one or more transfusions.

Local anesthesia is employed if the mental or physical distresses will not be too objectionable. Ethylene given under slightly increased pressure is the safest general anesthetic. The pressure prevents postoperative atelectasis. One stage may be done with local, the next with ethylene or as the patients elect, or operations may be begun under local and be completed under general anesthesia.

Resections begin with the uppermost or lowermost ribs according as they overlie the most serious lesions, and are repeated when the patient's condition warrants. The number of ribs resected at any stage should be one less than the patient can withstand. If the first operation or two introduces progressive improvement, others are postponed to make certain they are necessary. Undue delay is to be avoided as ribs regenerate and may require a second resection which is more difficult. Resection of the lower six or seven ribs may include all the periosteum and the intercostal muscles. Wound healing is excellent, and, after the edema disappears, the parietes which consist of the parietal pleura, skin and subcutaneous fat are soft and yielding. This permits of a wide range of adaptability and prevents interference with cardiac action by adhesions. Some patients are annoyed by being able to put a hand almost directly on their heart. It is not yet certain whether or not this prophylactic decompression of the heart is wise although it is harmless.

All ribs except the first and twelfth are removed from their angles to the sternum in complete thoracoplasty. If the paralyzed diaphragm is high, the eleventh rib is spared to assure saving the nerve supply to the upper portion of the rectus muscle. When conditions permit, the mesial portions of the five upper ribs are not resected to restrict deformity. Postoperative care includes transfusions, dextrose and salt intravenously, opiates and fresh air.

Failures.—Deaths are restricted to mistakes in selection of patients, to accidental wound infection and to acute pneumonia. Myocardial

incompetence limits subsequent activity. Lost morale may prevent repetition of resections needed to permit of healing or arrest of lesions.

Successes.—Proper selection and preparation of patients, restricting the number of ribs resected at any stage within limits of toleration and suitable after-care make thoracoplasty feasible for seriously handicapped patients. Performance of operations earlier, that is, as soon as it is probable that healing cannot occur until intrathoracic tension is appropriately altered, reduces both the number of ribs that must be resected and the period of convalescence. A larger proportion of patients can return to gainful occupations and, because their vital capacity is less curtailed, they are able to take positions that demand considerable activity. Many can resume their former vocations.

Proceeding in accordance with the plans outlined has made it possible to avoid fatalities from thoracoplasty, and no patient with a chance for recovery has been denied operation. This has been accomplished through cooperation with the medical men who have had direct charge of patients. Moreover, earlier and more general utilization of transfusions and induced paralysis of the diaphragm has reduced the number of patients who have needed rib resections and also the number of ribs it has been necessary to remove.

The problems incidental to tuberculous abscesses of the lung, cavities as they are usually designated, need solution which thoracoplasty does not provide. For example, an upper lobe may be converted almost completely into cavities and the balance of the lung remain quite unaffected, or, following a complete thoracoplasty, an abscess of considerable size may persist and continue to make mischief. Destruction of an involved lobe by the actual cautery as employed by Graham might be efficacious if sinuses did not persist. Were this procedure successful, it would be preferable to partial thoracoplasty. External drainage of abscesses already practiced by Lilienthal is perhaps more widely applicable than now seems probable.

SUMMARY

Prevention.—Pulmonary tuberculosis occurs because human, bovine and avian tubercle bacilli are deposited on the external and aerating surfaces of lungs and penetrate them to invade the parenchyma of such persons as are susceptible because they are unable to make suitable cellular and noncellular constituents of the blood.

Reduction in the number of bacilli now present in the air and ingesta is the primary requisite. The second is to improve living conditions. The third is to prevent reproduction of those whose hematopoietic structures are inherently weak.

Treatment.—The causes of the inception, the influences that govern the evolution of phthisis, and the factors that contribute to systemic and

pulmonary antagonism are fairly accurately established. Enough has been learned of how the factors can be modified so as to aid patients to recover or to arrest their disease to eliminate empiricism and routinism from phthisis therapy.

The procedures now available, nonoperative and operative, suitably and promptly utilized would diminish disabilities and reduce the present mortality rate more than has been hitherto possible. In addition to improving present procedures and a wiser utilization of them, the great obvious need is a potent antiserum.

GENERAL SUMMARY

Virulent tubercle bacilli are deposited so frequently on the external surfaces of the body from air, contacts and ingesta that every one is a carrier although most of the microbes do not survive. The surfaces are penetrated repeatedly with and sometimes without the provocation of superficial lesions. The bacilli enter the subcutaneous tissue and the gastro-intestinal and bronchial submucosa wherein some are deposited on the outer surfaces of blood capillaries and lymphatics.

Bacilli have now become invaders, and, being obnoxious, they arouse the antagonism of the host, namely, the increased activities of the adjacent tissue cells which are supported, reenforced and stimulated by the addition of cellular and noncellular constituents of the blood. A majority of the invaders are destroyed. The survivors are inactivated if the antagonism presented by the host is effective enough to confer insusceptibility, otherwise they maintain or regain their destructive activities according as the host, because of the degrees of inefficacy of antagonism, is more or less susceptible. A minority of surviving invaders remain in the subcutaneous and submucosal tissues and provoke or do not provoke lesions according as they maintain or regain activity or are reactivated. The others penetrate lymphatic and blood capillary walls or are carried into the lymphatics within wandering phagocytes.

Bacilli that enter blood capillaries after having penetrated the skin or the bronchial mucosa are transported in the venous blood and delivered through the pulmonary artery to the lung where most of them are deposited on the aerating surface, the endothelium of the capillaries of the lesser circuit. Bacilli that enter blood capillaries after having penetrated gastro-intestinal mucosa are transported in venous blood to the liver where most of them are deposited on the endothelium of the capillaries of the portal circuit within the liver.

Bacilli that enter lymphatics after having penetrated the skin are transported to adjacent regional glands and deposited on the endothelium of the intraglandular sinuses of the first or second gland. Bacilli that enter lymphatics after having penetrated the bronchial mucosa are transported to peribronchial glands or to hilum glands and deposited on the

endothelium of the intraglandular sinuses. Bacilli that enter lymphatics after having penetrated intestinal mucosa are transported with the chyle during active digestion through lymph glands, but not all are deposited on the walls of sinuses. The others are carried into the receptaculum chyli and promptly delivered through the thoracic duct into venous blood and thence to the lungs.

The bacilli that enter the venous blood of the systemic circuit, those that enter the blood of the portal circuit and are not deposited within the liver, and those that enter the blood with lymph in the thoracic duct are all delivered to the lung through the pulmonary artery.

Most of the bacilli in venous blood are deposited on the walls of the pulmonary capillaries, and the few that escape are disseminated throughout the body in arterial blood and deposited on the endothelium of the capillaries of the systemic circulation within every organ and tissue. Available evidence indicates that the larger proportion of invaders have penetrated the intestinal mucosa and are the more usual cause of pulmonary infection because they are frequently delivered promptly, directly or indirectly, into the venous blood.

This completes the first phase of invasion, namely, penetration of an external body surface, destruction and retention of some bacilli in submucous or subcutaneous tissues, dissemination of the balance through blood and lymph, and their deposition on the endothelium forming the aerating surface of the lungs, the digestive surface of the liver, the nutritional surface of every structure in the body, and the drainage surface (lymphatics) of all structures but the central nervous system, eye, internal ear and spleen which have none. Superficial and subsurface lesions are provoked if the surviving bacilli continue active in spite of antagonism; none, if they are inactivated by the antagonism of the host.

Subsequent phases of invasion are quite identical. Bacilli have been deposited on one of the surfaces (nutritional, drainage, etc.) of organs or tissues. The majority do not survive. Some of the survivors penetrate their internal surfaces and enter the parenchyma of organs and the cells of tissues instead of subcutaneous and submucous tissues. Again the majority are destroyed. Some of the survivors are retained *in situ* and may or may not provoke lesions. The balance are disseminated.

Organs particularly active in the physical and chemical filtration of blood and lymph (lung, liver, kidney, spleen and lymph glands) are the more often invaded and more liable to develop lesions.

Organs inactive in filtration (thyroid, muscle, brain, epiphysis of bones and fascia), whether they receive more or less blood, are less often involved and the less liable to develop lesions.

Every individual is invaded repeatedly, and presumably every organ and every tissue is invaded at one time or another.

Invading bacilli provoke lesions only if the antagonism of the host, provided by the responses of the cells of the structures invaded and the cellular and noncellular constituents of the blood, is insufficient to destroy or to inactivate the bacteria.

Responses of tissue cells contribute less to antagonism than to the cellular and noncellular constituents of the blood, and the noncellular constituents contribute more than the blood cells.

All contributions are essential to the development of the effective antagonism that provides insusceptibility.

Deficits in these contributions impose corresponding degrees of susceptibility.

Deficits in the noncellular constituents of the blood (namely, in the production of an abundance of sufficiently potent antibodies) are a constant factor imposing susceptibility; deficits in the number and stamina of blood corpuscles are a common factor.

Deficits in the effectiveness of responses of cells of tissues and of those forming the parenchyma of organs determine the location of lesions which are not limited to one organ or to a single tissue.

All forms of tuberculosis are systemic infections in which the predominant lesions occur in divers structures, e. g., lungs, genito-urinary and digestive tracts, lymph glands, bones, central nervous system, serous membranes, meninges, fascia, etc.

Pulmonary tuberculosis is the most common form of the disease because of the frequency of invasion by bacilli that have penetrated the external surfaces of the body and are disseminated through the blood, delivered to the lung through the pulmonary artery and deposited on its aerating surface.

Pulmonary tuberculosis is likewise the commonest serious concomitant or sequel of other forms of the disease.

Inception of pulmonary tuberculosis is attributable: first, to deficits in the constituents of the blood; second, to the frequency of invasion of the lung; and finally, to the inefficacy of the tissue responses, which are normally adequate but are often impaired by the scars of previous injuries and existing inflammations.

Treatment of all forms of tuberculosis includes improving the quality and restoring the volume of blood in circulation, increasing the volume of blood delivered, particularly to structures harboring the predominant lesions, restricting the activities of these structures to reduce dissemination of noxious products that cause the toxemia and of tubercle bacilli.

These measures are identical with the natural responses to focal and disseminated irritants which, when effective, produce spontaneous recovery and not infrequently confer insusceptibility. They should begin with recognition of the disease, even though it is incipient, and be con-

tinued after convalescence to obviate recrudescence or reinfection. Thus only will convalescence be hastened, disabilities be minimized and active life prolonged.

Treatment of pulmonary tuberculosis differs from that of other forms because of the peculiarities of the structure and functions of the lung and of its sensitiveness to alterations in tension.

Treatment of pulmonary tuberculosis cannot be fully effective unless operations (induced paralysis of the diaphragm, transfusions of unmodified blood and thoracoplasty) are added to other measures (rest, diet, fresh air, sunshine, etc.).

Application of pathology by the administrators of institutions, a further understanding of the potentialities and limitations of operation by internists and surgeons, and constant cooperation are requisite to progressive accomplishments.

CONCLUSIONS

Pathology and experience have defined therapeutic principles and indicated their application.

The incidence of all forms of tuberculosis will be materially reduced with reduction of the number of tubercle bacilli in the air and ingesta. Until this is accomplished wholesome methods of living, greater care in the selection, preparation and service of food, and the avoidance or correction of stasis and lesions in the gastro-intestinal tract are the most necessary preventive measures.

No form of tuberculosis can be cured in the sense that all bacilli can be removed from the body and reinvasion prevented.

Recoveries can be promoted for all forms of tuberculosis by augmenting the natural responses which lead so often to spontaneous recoveries.

In the treatment of pulmonary tuberculosis nonoperative measures alone and operative procedures alone cannot augment natural responses to their highest level of efficacy.

Prompt utilization of appropriate combinations of nonoperative and operative therapy is requisite to afford each patient the opportunity to achieve undelayed recovery.

Internists and surgeons who attempt to treat patients suffering from pulmonary tuberculosis are obligated to understand the potentialities and limitations of operative and nonoperative measures so that they may have the same working knowledge and differ only in the procedures they employ.

A common appreciation of the problems presented by each patient should promote study and investigation, prevent not only procrastination but also the subjection of patients to needlessly hazardous or crippling operations and to futile operations.

DIRECT DRAINAGE OF TUBERCULOUS PULMONARY CAVITIES

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Until comparatively recent years I had an idea that it would be dangerous, or at least unwise, to open deliberately a tuberculous cavity of the lung, as has been customary in nontuberculous abscesses.

While my experience is extremely limited, I am convinced that the danger of this procedure is not as serious as I had thought, and that great improvement may follow an operation of this kind. I had believed that openings into these cavities would never heal, and that the danger of hemorrhage was always present. Thus far, however, in three cases in my own practice, I have seen no hemorrhage, and the tendency toward the formation of a permanent fistula seems to have existed in proportion to the degree of collapse of the walls of the cavity. I do not here include direct bronchocutaneous stomas.

The cases in which this mode of surgical therapy should be selected are of two varieties: (1) those in which there is a virulent mixed infection with the clinical signs of pulmonary abscess, and (2) those in which a cavity cannot be collapsed without great danger to life and in which the accompanying sputum is so abundant that it threatens to spill into the opposite lung and to produce an extension of the disease.

Regarding the latter class, one must be fairly certain that the expectoration is coming from the cavity. This is not always so, for some cavities have a nonsecreting fibrous lining, and the discharge which appears as expectoration has its origin in other parts of the lung, often from bronchiectatic lesions.

There are two methods of draining these cavities: first, from the lung directly and, second, from the tuberculous cavity into an accompanying empyema, the condition thus being converted into one of pleuropulmonary fistula.

REPORT OF CASES

CASE 1.—Fanny S. was first seen by me five years ago, when she was 37 years old. At that time she had been ill for fifteen years with pulmonary tuberculosis. Soon after her first visit, a roentgen examination revealed extensive disease of the left lung with several cavities containing fluid (fig. 1), one of them as large as a small lemon near the hilum of the right lung posteriorly. There was some fibrosis with displacement of the mediastinum toward the more diseased side. The left lung was the seat of numerous healed lesions which had become calcified. There were no cavities here. Incidentally, she had enteritis, a perforated nasal septum following operation and a tuberculous disintegration of the right wrist.

The Wassermann test, suggested by Dr. James Alexander Miller on account of the perforated septum, proved negative. Dr. Miller agreed that the case was suitable for thoracoplasty.

On May 23, 1929, I resected the first five ribs, and three days later 400 cc. of whole blood was given (Dr. Nathan Rosenthal). Ten days after the first stage, I completed the thoracoplasty, resecting the remaining ribs including the tenth. Following this operation expectoration was greatly increased, the hemoglobin dropped from 85 to 60 and there was a distinctly septic picture. Roentgen examination now indicated that the cavities had been little or not at all influenced by an otherwise satisfactory collapse, so that two weeks later I operated again.



Fig. 1 (case 1).—Roentgenogram made before operation, showing two pulmonary cavities with fluid levels. Note the extreme retraction of the mediastinum including the trachea; the opposite lung is inactive.

At this time the patient seemed almost moribund. The wound was foul. Apparently there had been mechanical interference with drainage into the bronchial system. It was not necessary to cut ribs; I was able to attack the abscess directly through the wound, first passing a needle through extremely tough tissue, following the needle with a grooved director, and then divulsing with dissecting scissors.

The cavity proved to be bilocular (see two levels in fig. 1) with liquid pus in the lower chamber and mucopurulent material in the upper one. Feter was present. The septum between the two chambers was divided throwing them into one, and the entire cavity was packed with rubber dam. Four hundred cubic centimeters of blood was transfused by the citrate method. A chill with a tem-

perature of 106.4 F. followed, but proved evanescent. The following day the rubber dam was removed and replaced by a number of small soft tubes. As soon as convalescence was established the patient entered Loomis Sanatorium, but was obliged to return to New York in a few months because the wrist had broken down and was discharging tuberculous pus. I performed a typical excision of the joint with excellent and apparently permanent functional and cosmetic results, but the principal interest centered in the behavior of the pulmonary cavity.

At first it acted like a nontuberculous abscess of the lung with profuse anaerobic discharge. Then gradually the odor disappeared, and mucopus, looking much like tuberculous sputum, took its place. The cough rapidly diminished, and for a time completely disappeared. There was a gain of many pounds in weight, so that the patient instead of being rather emaciated became actually obese. The



Fig. 2 (case 1).—Roentgenogram made after several operations (see text). The pictures were made with Bucky's diaphragm. (The scattering of spots is due to faulty photographic technic.)

temperature was never high, but only occasionally reached normal. The cavity diminished in size, but refused to collapse completely. I began to think that I had reached a final result, when much to my surprise the fistula insisted on closing. Unfortunately, however, with this closure there was a recurrence of cough, although with little expectoration. About a year passed during which the patient felt well, but she was prevented from going about among her friends because of constant irritating cough with only a slight amount of sputum. This became so annoying that I resolved to make one more attempt to obliterate the tuberculous abscess. On March 19, 1928, with the patient under general anesthesia, I resected ribs to the outer side of the abscess and pressed the walls of the cavity together by packing a rubber dam between the wall of the chest and the cavity. An opening of fair size was left at the site of the old fistula, and I hoped that com-

plete obliteration would follow. The immediate result was excellent, and throughout the summer the patient felt well and coughed hardly at all, and I thought a final success had been achieved. Then she caught cold, and the accompanying cough seemed to force the cavity toward the right side of the chest and seemed also to enlarge it by the pneumatic stress of the strain of coughing. The wound, which had been entirely cicatrized, reopened, and something more will have to be done to recollapse the walls of the cavity. In the meantime there is a slight elevation of temperature, usually less than 100 F. maximum, but the cough has recurred. This case is recorded, not as an example of cure, but to show a good temporary result in a case which seemed hopeless. From past experience with this patient, I believe that the problem of final closure is mainly mechanical.¹

CASE 2.—G. R. M., a man, aged 37, was referred to me by Dr. Joseph L. Spruill of Jamestown, N. C. When he was first seen by me, there was an enor-



Fig. 3 (case 2).—Roentgenogram made before operation, showing enormous left apical cavity.

mous cavity of the left upper lobe, with tuberculous involvement of the lower left side of the chest as well, and an almost normal right lung (fig. 3). After several operations, including a complete thoracoplasty, a phrenic neurectomy and an apicolysis, the patient continued to cough and to show constitutional signs of the disease. I finally succeeded in collapsing the chest, but could not bring the walls of the large intrapulmonary cavity together. The best I could do is indicated in figure 4. Occasionally, roentgenograms showed a collection of fluid in this cavity, but as a rule it was apparently empty. In October, 1928, Dr. Amberson saw the patient with me; he said that he believed that the cavity was emptying into the lower part of the left lung and in this roundabout way was giving rise to the profuse expectoration. There was considerable cardiac deviation,

1. I expect to attempt closure by muscle flap implantation after a recent method devised by Pool and Garlock, soon to be published.

which perhaps accounted for much of the discomfort from which the patient suffered. Dr. Amberson strongly advised drainage of the cavity. The following day this was done, the patient receiving general anesthesia. It was necessary to incise the edge of the pectoral muscle near the middle of the scar following his apicolysis; the tissues were extremely tough, so that it was difficult to expose the walls of the cavity itself. This was eventually done, however, and a free opening was made, a number of necrotic plugs being wiped away with a sponge. When the cavity was opened, there was a sound of air rushing in or out, but after that no sounds indicating a connection with a large bronchus were heard, nor was there any bleeding at the patient's mouth. The finger exploring the



Fig. 4 (case 2).—Roentgenogram made after several procedures, including avulsion of the phrenic nerve. The cavity has been finally incised for drainage.

mesial wall of the cavity was so close to the aortic arch that no intervening tissues could be clearly appreciated. A large opening was made from the top to the bottom of this cavity. A roentgenogram made with the cavity packed with iodized oil gauze demonstrated that the gauze was actually within the lung. The discharge was fairly free, but was not copious. There was gradual improvement, and the patient went to his home. Later cough and expectoration almost or quite disappeared. Then he "caught cold," and the discharge both by mouth and through the wound increased.

One of the important and interesting points in this case is that in spite of my having widely opened this large tuberculous cavity, it was

impossible to maintain a free opening, and now the fistula is represented by a tiny, only slightly discharging aperture. The patient is at present at Loomis Sanatorium, where he continues to improve. The right lung has not changed since I first saw him and is in good condition.

The next case is of great interest because I believe that the procedure employed is one which should be followed in many cases of tuberculous empyema without pleuropulmonary fistula, and in which thoracotomy does not check the cough with its copious expectoration.

As I have suggested, it is generally conceded that profuse discharge through the upper air passages tends to implant the disease in the other lung. I am well aware that many cases can be cited in which prolonged expectoration of this kind has not been followed by contralateral extension, but these are not the ones which should guide one in treatment. It is the unfortunate spreading of the disease which therapy should prevent.

It seems to me that in deciding on operative treatment, one should consider the possibilities of a fatal issue if nothing is done rather than the mere cure of a condition which does not directly threaten life.

As an example, take chronic abscess of the lung. A surgical procedure looks dangerous because the disease may not be at once menacing, but when there are massive hemoptyses or a sudden extension of pulmonary gangrene it may be too late for surgical assistance. It is to prevent such possibilities that operation is advised rather than merely to check the annoyance of cough and expectoration. This principle is a general one and is by no means confined to thoracic surgery.

A method for dealing with open pyopneumothorax with profuse expectoration from the diseased side was suggested in this case by Dr. J. Burns Amberson, Jr., and I cannot do better than present a brief résumé.

CASE 3.—M. C., a man in the forties, who had been ill for many years with bilateral pulmonary tuberculosis, presented dense infiltration with cavitation in the entire right upper lobe with less marked infiltration below. There was infiltration just outside the hilum of the left lung as well. The right side of the chest was treated by artificial pneumothorax, and while this was efficient below, the adhesions about the upper lobe were so dense that the capacity of the cavities was not influenced by the pneumatic pressure. The left lung meanwhile became "dependably quiescent." Fluid developed in the right side of the chest, and could not be eliminated in spite of aspiration and the injection of disinfectants.

Paravertebral thoracoplasty was performed with only partial success, the pleura being extremely dense and tough, so that full collapse was impeded.

Anterior rib resections were also performed, but with little effect. Then I attempted to compress the upper lobe by apicoylsis, and during the operation entered the pleura, which contained a large quantity of sanguinolent fluid. This, naturally, became infected, and a low thoracotomy for drainage had to be performed.

After every procedure the patient had a severe reaction, so that in spite of the large number of operations I approached each one with trepidation. Finally, although drainage from the thoracic fistula was free, the patient expectorated

more than 6 ounces a day from the cavities in the upper lobe. There was gradual decline, and I greatly feared that the left lung would become seriously involved and that he would die. It was then that Dr. Amberson saw him and made the suggestion that I should freely enter and expose the pleural cavity and deliberately open the lung so that the patient would expectorate into his pleura instead of through his mouth.

This procedure was undertaken on Jan. 5, 1928. Nitrous oxide and oxygen were administered by Dr. Branower. The operation proved more difficult, technically, than I had expected. I incised through the old posterior scar and exposed the ribs, which had become united by bony bridges of such ivory hardness that I had to use the chisel and mallet for most of the thoracoplastic work. Six ribs were thus divided as close as possible to the spine as well as in front of the cicatrix, and this entire part of the cuirass, consisting of six ribs united by bone, was removed in one piece. The pleural cavity was thus entered and a rib spreader applied. The exposure was perfect. The lung below the apex was found compressed into the spinal gutter by a leather-like investing membrane.

The adhesions of the upper portion of the upper lobe had to be severed from the wall of the chest with a heavy knife before the lung could be freed further with the fingers. I succeeded in peeling it entirely away from the dome of the pleura, and then attempted to locate the cavity from which the sputum was supposed to have come. There was no appreciable cavity, however, and I feared that I might be in danger of entering the trachea at this level. I decorticated this part of the lung of its leathery pleura; there was immediate collapse of the pulmonary tissue, which seemed to become a carnified contracted mass, and which at once moved down into the spinal gutter. This lung did not move on expiration nor expand with intrapharyngeal air pressure. I freely incised it, and small quantities of pus escaped. I then closed the wound in the chest with chromicized catgut sutures, leaving the skin open, however, and also leaving a space for packing so as to hold the lung against the rigid mediastinum. For the packing I used rubber dam and gauze. I then closed the skin with silkwormgut sutures in mattress fashion.

Transfusion with 800 cc. of citrated blood was then performed.

Following this operation there was, as might have been expected, considerable reaction, but the cough was greatly diminished, and there was almost no expectoration.

In this case one sees an enormous wound, extending directly into thickened pleura, tuberculous for many years. Healing was necessarily slow, and it was not until nearly three months later that the patient was well enough to be transferred back to Loomis Sanatorium. Under a careful hygienic regimen, including forced feeding, there was continued improvement, so that in the following autumn he returned to his home in Cuba. He has progressed satisfactorily ever since. The little sputum which he continues to expectorate has been reported negative by two laboratories in Havana. This, of course, is not to be taken as a sign of cure; it merely signifies that the disease is less active than it was.

The patient is up and about, although there are two small drainage fistulas: one in the lower part of the chest, and the other, a small, slightly discharging sinus, in the axillary region.

I report this case because I am convinced that the method should be employed more frequently when there is a closed pulmonary cavity discharging infected sputum by mouth and when there is an open tuberculous empyema.

SUMMARY

1. Two cases are reported in which improvement followed direct drainage of a tuberculous pulmonary cavity through the wall of the chest.

2. One case is reported in which an apical cavity discharging copiously by mouth was drained into an open pleural tuberculous empyema.

CONCLUSIONS

1. Improvement has followed the surgical drainage of tuberculous pulmonary cavities whether directly through the wall of the chest or into an open empyema.

2. The dangers of contralateral infection by implantation are diminished by the drainage of copiously secreting pulmonary cavities.

3. There is a strong tendency toward spontaneous healing of surgical openings into tuberculous cavities in the lung.

PHRENICECTOMY IN THREE HUNDRED CASES OF PULMONARY TUBERCULOSIS

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It is not my purpose to go into the history of the surgery of the phrenic nerve, nor to review the literature on phrenic exeresis in the treatment of pulmonary tuberculosis. I desire merely to report the results in a series of 300 such operations, done on all types of tuberculous patients, and to determine what conclusions can be drawn as to the value of the procedure.

The operation is simple, involving division or crushing of the phrenic nerve in the neck in order to produce permanent or temporary paralysis of the diaphragm on one side. It is done under local anesthesia through an incision about an inch long placed accurately in one of the transverse folds of skin about an inch above the clavicle and with its center over the anterior scalene muscle which lies beneath the outer border of the sternomastoid. This incision gives a much less conspicuous scar than the vertical one, and in my experience, affords a more satisfactory approach to the nerve than the low one practically on the clavicle. If a temporary result is desired, the nerve is simply crushed with hemostatic forceps for about a fourth of an inch as it crosses the scalene muscle. If the accessory branch can be found, this is also crushed. Paralysis is obtained promptly, but function returns in from five to six months. To secure a permanent result, the nerve is divided, the lower end seized with forceps and by steadily pulling and twisting, several inches of nerve are evulsed. Often the whole nerve comes out, but a permanent result is obtained if only sufficient length is removed to assure breaking of the accessory attachment. This method of exeresis has always impressed me as being much simpler than the operation of Goetze, which involves the isolation and section of the accessory nerve.

Following operation, the hemidiaphragm rises about 2 inches (5.08 cm.) above its normal position and either remains stationary or has a slight paradoxical motion during respiration.

As to indications for the operation, my ideas have changed considerably with experience. At first it seemed natural to suppose that the procedure was best suited to basal lesions of the lung, and in Saranac Lake the first phrenicectomies were done in cases of this type. Gradually, and more or less experimentally, the operation was done in cases of upper lobe or apical lesions, and my co-workers and I were rather surprised to find it giving good results more often than in the cases in

which the lesions were in the lower lobe of the lung. The operation is now employed in all types of lesions. Naturally, it is used chiefly in unilateral cases, without regard to the lobe involved.

O'Brien¹ of Detroit has given a list of indications which agrees essentially with ours: namely, cases in which the patients are not doing well under ordinary rest treatment, but which are not considered sufficiently advanced for the use of artificial pneumothorax; cases in which pneumothorax has been attempted and found impossible on account of pleural adhesions; cases in which cavitation has occurred but in which thoracoplasty is not yet indicated; cases in which thoracoplasty is to be done and phrenicectomy is to be used as a preparatory measure; and



Fig 1—The roentgenogram on the left shows a large apical cavity before phrenicectomy, on the right, the same case after phrenicectomy with the cavity nearly closed.

finally, those cases in which the patients obviously need thoracoplasty but are poor risks, yet in whom we hope to get sufficient improvement following the operation on the nerve to prolong life, or ease symptoms, such as persistent tiring cough, with the possibility in mind that the more radical procedure may be attempted later.

The statistical results of the present series are as follows: Three hundred operations on the phrenic nerve are included in the study. As it was desired to determine the results of phrenicotomy only, twenty-three of the cases in which thoracoplasty had been performed subsequently

1 O'Brien, E. J.: Surgery of the Phrenic Nerve and Intrapleural Pneumolysis, *J. A. M. A.* **92**:463 (Feb 9) 1929.

were left out of further consideration. Six of the patients have not been traced; so the total number on whom results have been checked is 271. Of these, 173, or 64 per cent, were improved by the operation, and 98, or 36 per cent, were not benefited.

The cases listed as improved vary from those in which the patient merely had some slight symptomatic improvement such as a decrease in cough or expectoration, or a lowering of temperature, to those who have been greatly benefited, with marked changes in the roentgen observations, diminution or actual obliteration of cavities, and complete disappearance of all symptoms. The list of failures includes a considerable number of hopeless cases in which the operation was done with faint

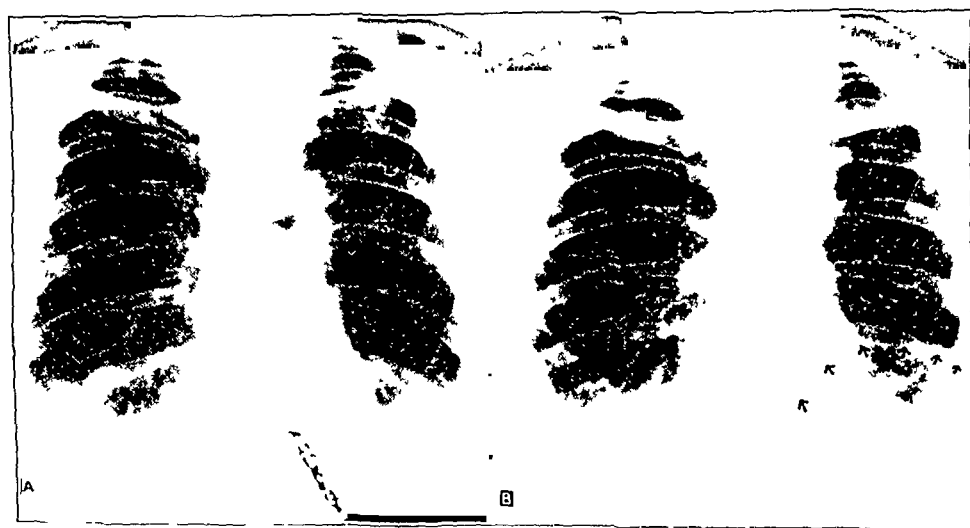


Fig. 2.—The roentgenogram on the left shows a multilobular cavity in the upper lobe of the left lung before phrenicectomy; on the right, the same case after phrenicectomy with the cavity closed.

hope of securing a good result. If these were deducted from the list of failures, the number of good results would be well over two thirds of the total.

In 1927, an analysis of our first hundred cases was made in the hope of finding a way to predict the result in any individual case from a previous examination of the clinical signs and the x-ray pictures. The present analysis of 300 operations is a continuation of the same study. We had hoped by this time to be able to give a fairly accurate prognosis and to be able to say with some assurance that the operation will help one patient and that it will not help another. In this hope we have been disappointed. In one case the operation will be promptly followed by

a contraction or complete disappearance of a good-sized apical cavity, with corresponding lowering of temperature, reduction of cough and expectoration and general improvement. We have had many cases like this; patients who have been steadily growing worse and whose cavities have been gradually enlarging in each succeeding x-ray picture up to the time of phrenicectomy, and who have thereafter gone on rapidly to a practical clinical cure. We operate on other patients with the same type of lesion, the same clinical progress and the same x-ray picture and get no improvement.

We do feel, however, that we can offer the operation to the patient with a reasonable assurance that it will do no harm, even if it fails to give any decided benefit. In 300 cases, we have had only five patients or less than 2 per cent, who have been made actually worse. Four of these five had basal cavities, and whether the rising diaphragm interfered with drainage or had some other effect, we do not know.

Few patients have any annoying dyspnea after the operation. In the few who do, it is usually of short duration. In a small number the rise of the diaphragm has been followed by digestive upsets, but the majority of these have been temporary. They have been no more common following left than right phrenicectomies. A small number have had a persistent tachycardia following operation—a rise in pulse rate from 10 to 20 beats per minute. This phenomenon I have been unable to explain, as the vagus nerve is never touched.

Only one accident has happened in the whole series of cases. In one of the early operations performed on the left side, the thoracic duct was cut completely across. For twenty-four hours there was a profuse flow of milky fluid from the wound, but a simple gauze packing stopped it, and there was no after-effect pointing to a loss of chyle from the blood stream. There has been no case of serious hemorrhage during the operation.

One interesting case involving bilateral phrenicectomy is included in the series. The patient was a man, aged 67, who came to Saranac Lake with a far advanced pulmonary tuberculosis of the left lung, chronic myocarditis and dyspnea. He had been hiccuping for long periods at a time for the preceding three months. A left phrenic exeresis was done in the hope of checking the hiccup. He had relief for twenty-four hours and then began again. One week later he called me in and asked me to cut the nerve on the other side. I explained the seriousness of the procedure and warned him that it might be fatal. He insisted, however, arguing that he was sure to die soon from exhaustion if the hiccups were allowed to continue. I consented and with considerable trepidation exposed the right phrenic nerve and crushed it. There was no increase in dyspnea and the hiccups ceased, only to begin again the

following day. I had made no attempt to crush or sever the accessory phrenic nerve on the right. The patient then ordered me to make a complete section. I operated once more six days after the crushing and did a radical exeresis on the right. Again there was no change in the breathing and the hiccups stopped permanently. The man lived for two weeks, and then his heart finally gave out. Both the persistence of the hiccup after exeresis on one side and crushing on the other, and the absence of increased dyspnea after complete paralysis of both diaphragms were interesting.

A number of experiments have been carried out in the use of phrenicectomy as an accessory to artificial pneumothorax. Several

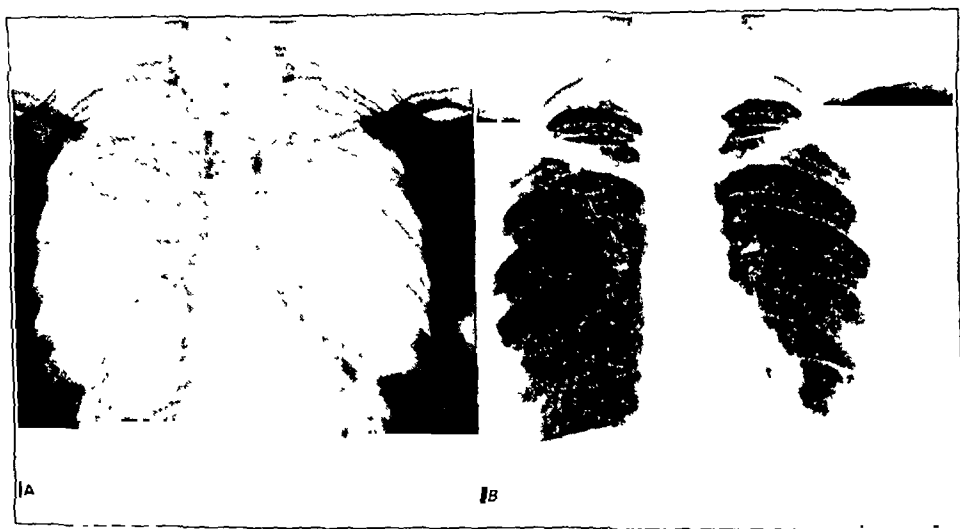


Fig. 3.—The roentgenogram on the left shows bilateral apical cavities; on the right, the same case after left phrenicectomy with the left cavity completely gone and the right cavity greatly reduced in size.

years ago Alexander expressed the opinion, based at the time on theoretical reasoning, that diaphragmatic paralysis would be of distinct advantage in nearly every case of pneumothorax. He thought that it would lengthen the time between refills, decrease the chances of fluid, and by diminishing the thoracic volume, make it easier for the reexpanding lung to fill the chest completely when the pneumothorax was finally discontinued. In the main, our experiences in this line have been unsatisfactory, *although it must be admitted that the number of cases of pneumothorax in this series is relatively small.* I have seen one striking case illustrating Alexander's first point. A man who had a satisfactory collapse but who had to have gas promptly every nine days, was able

to go comfortably for three weeks or more between refills after phrenicotomy. In most of our other cases, however, there has been no beneficial result, even when there has been an adhesion from the lower lobe to the diaphragm which seemed to be interfering with satisfactory collapse. As a rule, the rise of the diaphragm in these cases is slight or absent. Whether there is any lessened tendency to fluid, I do not know.

Although I believe that the cessation of motion in the diaphragm is a more important factor than its actual rise into the chest in bringing about a good result, I do not believe that lack of motion before operation as observed by the fluoroscope is a contraindication to phrenicectomy. The clinical results are satisfactory in many cases of this type.

In six of twenty cases in which the nerve was crushed the patients were subsequently reoperated on and the nerve was extracted. These patients showed definite improvement for about five months and then began to relapse. In no case was there any difficulty about finding the nerve at the second operation.

I believe fully in the use of the operation as an accessory to thoracoplasty. It gives a better collapse and often does away with the necessity of removing the tenth rib.

CONCLUSIONS

Paralyzing the hemidiaphragm by evulsing or crushing the phrenic nerve is a simple procedure which is of distinct value in a wide variety of cases of pulmonary tuberculosis. Its value is fully as great in cases of apical lesions as in those in the lower lobe of the lung.

The operation gave beneficial results in approximately two thirds of a series of 271 cases.

Less than 2 per cent of the patients seemed actually made worse, so that it is reasonably safe to assure them that no harm will come of the operation even if it fails to do good.

THE ELECTROSURGICAL METHOD OF CLOSED INTRAPLEURAL PNEUMOLYSIS IN ARTI- FICIAL PNEUMOTHORAX *

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It is generally admitted that artificial pneumothorax is not only the most widely applicable method of collapsing the lung in the treatment of pulmonary tuberculosis but also the most valuable. Unfortunately, pleuritic adhesions are almost invariably present in cases in which the patients require pneumothorax treatment and constitute the greatest obstacle to a satisfactory end-result.

As a result of experience in the treatment of approximately 1,400 patients with pulmonary tuberculosis with artificial pneumothorax during the past eighteen years, my co-workers and I are convinced of the importance of establishing a type of pneumothorax which within a few months will give the diseased lung sufficient functional rest, collapse or compression to render it no longer a source of tuberculoxemia or tubercle bacilli-laden sputum.

The importance of a satisfactory collapse of the lung is strikingly shown in the accompanying table. A careful review of the clinical records and stereoroentgenograms in 245 cases in this series reveals that the primary cause of failure of treatment with pneumothorax in 40 per cent of the cases was the presence of adhesions, which prevented a satisfactory collapse of the lung. In most of these cases, a temporary improvement followed pneumothorax treatment in spite of insufficient collapse of the lung. Consequently, the treatment was continued sometimes for prolonged periods, in the hope of stretching the offending adhesions and securing a good collapse of the lung. Sooner or later, however, either extension of disease took place to the opposite lung, intestines or throat, or some complication as empyema, spontaneous pneumothorax or obliterating pneumothorax occurred, compelling discontinuation of pneumothorax treatment. Unfortunately, the cases were then too far advanced to utilize other methods for collapse of the lung.

While adhesions are present in the majority of patients selected for pneumothorax treatment, according to our experience, a satisfactory pneumothorax can be established in 40 per cent of the cases.

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In a similar percentage (40 per cent), however, the character of adhesions will prevent the necessary collapse or compression of the lung to provide adequate functional rest or closure of cavities; and in the remaining 20 per cent, pleuritic adhesions will prevent any introduction of gas. Thus, pneumothorax treatment will prove efficient in considerably less than half the cases wherein it is indicated.

The phthisiotherapist recognizes the value of thoracic surgery. In those cases wherein no gas can be introduced, he now more often takes advantage of the surgeon's ability to bring about collapse of the lung by a phrenic neurectomy or thoracoplasty instead of subjecting the patient to prolonged and unsatisfactory sanatorium care. However, the fate of cases presenting pleuritic adhesions, which prevent efficient collapse of the lung, leaves much to be desired.

The usual procedure in cases of this type is to keep up the pneumothorax frequently, month in and out, and sometimes even year in and

Comparative Value of Artificial Pneumothorax in Cases in Which Adhesions Did Not Prevent Adequate Functional Rest and Closure of Cavities, and Those in Which Adhesions Did Prevent Sufficient Collapse of the Lung to Close Cavities or Give the Necessary Functional Rest

Observations on 850 Cases Jan 1, 1911 to Aug 1, 1925			
Character of Pneumothorax	Clinically Well, Per Cent	Arrested Per Cent	Dead, Per Cent
Satisfactory collapse, adhesions not preventing closure of cavities or adequate rest of the lung	48	20	21
Partial collapse, adhesions preventing satisfactory closure of cavities or adequate rest of the lung	13	13	50

out, especially if there has been some reduction in the quantity of the twenty-four hour sputum or its germ content, or if the patient has made some clinical improvement in spite of roentgenograms showing definitely that adhesions are preventing a satisfactory collapse of the lung. Admittedly, a small percentage of the patients in such cases recover, but the vast majority do not. The greatest indictment against the phthisiotherapist today, aside from not using collapse therapy as a whole to the extent it is indicated, is the continuation of a useless pneumothorax for prolonged periods, denying the patient the advantages of other recognized operative procedures.

Opinion will differ, of course, as to what constitutes a satisfactory pneumothorax. However, it is not to be decided only by the degree of collapse or compression shown in the roentgenogram, nor by the mere presence or apparent absence of adhesions per se. In one case, there may be only a thin layer of gas between the lung and the chest wall and the pneumothorax may be satisfactory, while in another case, there may be an enormous pneumothorax with displacement of the mediastinum, heart and diaphragm and with little lung tissue visible;

and yet, because of an uncollapsed cavity held open by adhesions, the patient may continue to expectorate sputum containing tubercle bacilli. It is a common observation of every phthisiotherapist that a single string or slender band adhesion extending from the partially collapsed lung to the thoracic wall frequently holds open a cavity and renders pneumothorax treatment a failure.

As a result of our experience, we have become convinced that pneumothorax will not give a satisfactory end-result if, after several months' trial, stereoscopic films reveal the presence of adhesions, the nature of which is preventing sufficient collapse of the lung or compression to bring about a satisfactory reduction in the amount and bacilli content of sputum from the diseased lung.

Careful roentgenologic study of adhesions in pneumothorax will show that they are more often distributed over the more diseased parts of the lung, being found almost invariably over superficial cavities. Consequently, the very part of the lung which is in greatest need of collapse is the least likely to receive it in an adequate measure.

Early in our experience with pneumothorax, we recognized the necessity of a satisfactory pneumothorax, but considered open operations or closed operations with the original Jacobaeus instruments too dangerous. We advocated instead that the adhesions be stretched by increasing the intrapleural pressure in order to secure a good collapse. Study of our end-results shows that this method was unsatisfactory, because not only did we seldom get a good collapse, but spontaneous pneumothorax was 40 per cent more common in cases in which we had resorted to the stretching of adhesions. The marked increase in spontaneous pneumothorax was undoubtedly due to tearing of the parenchyma of the lung or liberation of tuberculous foci from torn adhesions.

Four years ago, after Unverricht had developed his new thoracoscope, we again adopted the method of closed pneumolysis in all suitable cases. The general impression among phthisiotherapists and surgeons is that few cases are suitable for the operation. In studying the clinical records of stereoscopic films in ninety-one cases in a former series of patients now dead in whom adhesions prevented closure of cavities, we found that 40 per cent were suitable for pneumolysis early in their pneumothorax career; had they been operated on instead of being subjected to prolonged pneumothorax treatment, probably 50 per cent would be alive and well.

The value of the closed method of pneumolysis seems, by many, to be the least appreciated of any of the methods for collapse of the lung. This procedure is neglected for two reasons: The phthisiotherapist generally lacks the necessary surgical training and judgment, while the surgeon frequently lacks clinical experience in tuberculosis and

knowledge of pneumothorax as a background. Both are unwilling to spend the necessary time to perfect the technic. Thus, the surgeon favors the open method of pneumolysis, or thoracoplasty, while the phthisiotherapist clings to his partial pneumothorax. Both fail to appreciate the improvement in the technic of cutting adhesions, and many still retain the impression that it is dangerous.

These dangers are largely technical. Formerly, one worked pretty much in the dark with poor instruments and equipment. We, ourselves, went through this period and gave up the method, as we considered it dangerous and of little utility. Today, however, we have improved instruments and a more refined technic, and while the operation may be technically difficult, it is at least not dangerous when properly done.

If collapse therapy is indicated, it is our policy to try artificial pneumothorax. If a satisfactory collapse of the lung is not obtained within a few months, and it is shown on serial stereoscopic films that adhesions are preventing a satisfactory collapse, we consider a pneumolysis at once.

During the past four years, the patients in 45 per cent of our cases in which there was unsatisfactory collapse have proved suitable for the operation. If not suitable, we consider other methods of collapse instead of continuing a comparatively useless pneumothorax.

The technic, indications and contraindications for intrapleural pneumolysis, as well as the selection of cases and end-results, have been covered in a previous contribution.¹ It was pointed out in a former communication that the cauterization of adhesions by the galvanocautery is objectionable because of the heat, smoke, pain and reaction to operation. Perhaps its greatest shortcoming is the character of the cutting produced because tissue is destroyed for a short distance around the cautery. Thus, blood vessels are severed without any previous obliteration, and unless a dull red heat is used, undue bleeding may occur. In addition to these reactions, if too much heat is used, there is also the danger of tissue necrosis occurring, which may involve the parenchyma of the lung, tuberculous cavities or tuberculous foci, thus liberating infection, or the necrosis may invade blood vessels and cause serious secondary hemorrhage. Furthermore, while the time required for the cautery to heat and cool after the current is thrown on or off is short, it nevertheless has its disadvantage, as occasionally a moment's delay, rendering the cutting instrument active or inactive, may result in serious consequences. Moreover, the shaft of the cautery sometimes becomes extremely hot and may cause a sloughing at the point where it passes through the thoracic wall. The hot cautery shaft may also damage lung

1. Matson, R. C.: Cauterization of Adhesions in Artificial Pneumothorax by the Jacobaeus-Unverricht Method of Closed Pneumolysis, *Am. Rev. Tuberc.* **19**: 233 (March) 1929.

tissue or the pericardium on which it may rest, during operation, unobserved by the operator who is giving his attention to the cutting alone.

All of these difficulties and dangers were serious, objectionable features which prevented successful results in many instances.

The successful utilization of electrosurgical methods in operations on the brain and in treatment for cancer stimulated much experimentation on our part to apply these methods to intrathoracic surgery, in an effort to lessen the difficulties and reduce the hazards incident to the use of the galvanocautery. We applied the electrothermic principle for the severing of adhesions, and as a result of its advantages over the galvanocautery, we are utilizing electrocoagulation and cutting in all cases presenting the difficulties that we have outlined.

During the utilization of this new principle over a period of the past two years, we have repeatedly performed operations by this method which would not have been attempted with the galvanocautery, and the comparative safety of the method over the galvanocautery procedure, with the results obtained, have created a strong conviction that the electrocoagulation and cutting will replace the galvanocautery. The application of the method intrathoracically, however, involves difficulty of control of bleeding not present in any open operation. While hemostasis in an open operation can be obtained by well known and easily applied surgical methods, it is obvious that these same procedures cannot be applied in such operations as the closed pneumolysis.

Aside from the anatomic relationship of large blood vessels and important nerve trunks to pleural adhesions or to the pericardium, it is of vital importance to know whether the adhesion to be cut contains blood vessels, compressed lung tissue, diseased foci or the prolongation of a cavity. Cutting into the prolongation of a cavity or compressed lung tissue is avoidable. Cutting into tuberculous foci in adhesions can be efficiently dealt with; but hemorrhage is one complication not always avoidable, and if it is at all profuse, it is a most unpleasant experience for the operator.

It is my prime purpose in this paper to discuss the utilization of electrosurgery for cutting adhesions in artificial pneumothorax by the closed method under thoracoscopic control, with especial reference to control of bleeding.

It is to be hoped that this paper will not encourage those without experience in this new branch of surgery to undertake too difficult operations at first, as the operation might result in failure and thus bring about unjust criticism of an otherwise valuable procedure. One sometimes hesitates, therefore, to describe a new technic, as it may make inexperienced operators too venturesome.

The usual source of bleeding during the process of cutting adhesions is from blood vessels collateral from the intercostals. One meets with

two types of vessels: those situated subpleurally, which can usually be detected by thoracoscopic examination and easily controlled, and those situated in the interior of adhesions, from which profuse bleeding occurs at times. In the case of the former, bleeding may be easily controlled by electrocoagulation; or, if the galvanocautery is used, before the blood vessels are cut they may be thrombosed by the application of the flat surface of the cautery. Dangerous bleeding, however, comes from blood vessels situated in the interior of adhesions, particularly in those which are dense and well organized. This dense type of adhesion is found in cases in which the patients have been subjected to prolonged and sometimes even short periods of pneumothorax treatment, particularly if the patient is of a fibroplastic constitution with a tendency for productive changes to take place in the tissues following pneumothorax treatment.

The latter type of vascular adhesion is more often found in the costovertebral gutter, at the apex of the lung and anteriorly near the costochondral junction. Densely organized adhesions in these areas should be approached cautiously because blood vessels of considerable size may be situated in their interior, the presence of which is not always possible of determination until they have been cut into.

Bleeding occurring during the cutting of cord and band adhesions, if the adhesions are not densely organized, usually stops after the adhesion has been cut through and the stump contracts. In well organized tissue, however, little retraction takes place, and bleeding may be a source of considerable anxiety to the surgeon. Therefore, it is obvious that the ideal method of severing adhesions must provide efficient hemostasis.

The objections to the galvanocautery in connection with hemostasis have already been pointed out. A detailed description of the physical characteristics of currents employed in electrosurgery will not be discussed. However, an understanding of the effects of the high frequency currents employed in the electrothermic method of cutting adhesions is necessary to apply this new procedure intelligently.

Briefly, the cutting effected by the electrothermic method is not a true cutting but a molecular disintegration of the tissues produced by a high frequency undamped current, an arc being formed at the point of contact between the tip of the electrode and the tissue.

It has been found that the form of high frequency electric current which results in the best cutting of tissue with least charring is that generated by the utilization of thermionic tubes used in radio broadcasting, which give sustained oscillations of uniform amplitude at a rate of 600,000 per second. Even with an apparatus generating this form of current, it will show an impairment in cutting if the rate of oscillations is considerably increased or decreased. Based on this rate of oscillation, the theory is advanced that the cleavage of the tissue is accomplished not by mechanically cutting or by cauterization, but by a cellular disruption

resulting from the reaction of the cells to a sustained vibration transmitted at their own inherent vibration rate. The little sparking and resultant film of coagulation is secondary and subsequent to the cleavage of the tissue. Thus, two separate and distinct functions may be observed. One is the transmission by the operating electrode of the oscillations to cause cleavage, and the other is the slight sparking as the needle breaks contact with the parted tissue. If properly adjusted and handled, this results in a slight film or coagulation sufficient to check capillary bleeding but not sufficient to cause sloughing or charring with the danger of subsequent hemorrhage.

The ideal current for cutting, therefore, is recognized as that having a uniform sustained amplitude of 600,000 oscillations per second.

On the other hand, the best form of high frequency electric current for the generation of heat as used in coagulation is that having a damped oscillation of a long decrement. This current is generated from suitable apparatus containing spark gaps, condensers, etc. An apparatus properly designed delivering currents having long decrements will result in a clean blanching and dehydrating of the tissue when properly applied for coagulation, but apparatus of improper design may have a short decrement of the oscillating currents which will result in a brown or black burning of the tissue when applied for coagulation. The rate of oscillations of this form of current is usually about 1,250,000, but the rate of oscillation is not so important as the form of the trains or the decrement.

Two distinctly opposite forms of current are utilized in electro-surgery: One is ideal for cutting and the other for coagulating. To get the best results, it is essential to employ apparatus furnishing these two forms of current obtainable at the will of the operator and in the strength suited to the work. There are devices which will deliver cutting characteristics from a generator by means of a spark gap. This current, however, is a compromise between the two ideal currents and consists usually of a damped oscillation having short decrement and having the trains of oscillation crowded together. The peaks of the resultant current may simulate the oscillations of the undamped oscillations, but there are present the superimposed short oscillations which tend to cause undue heating when used for cutting. Similarly, this form of current even when differently adjusted is far from the ideal for coagulating. In practice, apparatus delivering the latter form of current is likely to be somewhat erratic and require adjustment from time to time in the course of operation. In other words, there is no assurance that it will respond to the requirements of the moment. In important surgical work, when hesitation, delay or trial cannot be tolerated, obviously nothing but the ideal currents for cutting and coagulation should be employed.

In our work, we have utilized the Wappler Wyeth Endotherm with special instruments which I have designed for intrathoracic use (fig. 1).

In the use of the coagulating current, a blunt electrode held in contact with the tissue and a small amount of current turned on will result, within a few seconds, in a blanching, dehydrating or coagulation in a circle around the blunt point. This will expand until the process near the point is carried to the degree of burning which would be manifested in a little sparking and by the formation of carbon. Obviously, it is desirable to stop before that state has arrived. On cutting through the center of this coagulated area with the operating electrode, it will be found that the depth of the coagulation is about equal to the radius. Thus, in using the blunt electrode, the area of the visible destruction may be used as a gage of its depth. Coagulation may be employed for hemostasis, if necessary, by clamping the tissue or vessel with the intrathoracic hemostat and switching on the coagulating current.

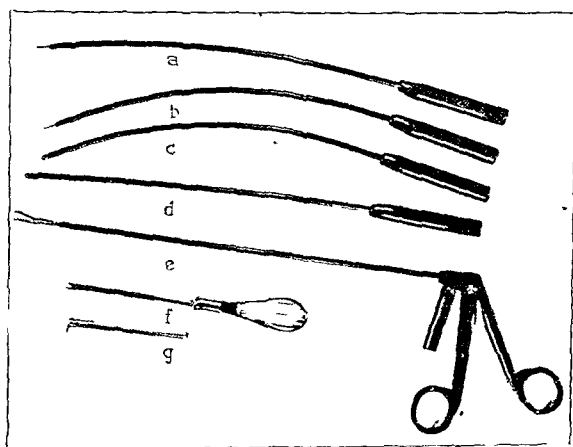


Fig. 1.—Author's instruments for the electrosurgical method of cutting adhesions: *a*, cutting electrode; *b*, pointed electrode for electrocoagulation; *c* and *d*, blunt electrodes for electrocoagulation; *e*, intrathoracic hemostat; *f*, trocar, and *g*, flexible cannula.

In the use of the cutting currents, considerable practice, first on meat and later on live animals should be exercised before an attempt is made to use them on the human body. In practice, it is best not to apply to the tissue to be cut more than a short portion of the operating electrode, the tip or only a few millimeters of the edge. If a larger portion is used, it will impair the cutting quality. Neither pressure nor traction should be used; in fact, this is objectionable. The operating electrode should be merely touched against the tissue, preferably at the point, and the action is that of following through the cleavage thus made. A little practice is required to get the sense of touch which is entirely different from that of traction or pressure of surgical cutting.

The amount of coagulation on the incision walls depends on the relation between the strength of the current employed and the speed of the passage of the electrode across the tissue. A little experimentation will soon teach the nature of the results expected. For example, with the cutting strength set at number 3 of the selective switch of a Wyeth Endotherm, an incision can be made at a fairly rapid rate without more than the film of coagulation, whereas hesitation or slow movement would result in charring. If slow movement is necessary, the cutting strength should be cut down to avoid charring. To make deep incisions, it is better to avoid attempts to make them with one stroke but rather to go over the same incision again using the point of the operating electrode and avoiding further contact with the tissue already parted. If bleeding spots show up after cutting by the proper current, the apparatus may be switched over to the coagulating current and the bleeding spot "touched up" with the operating electrode sufficiently to check the bleeding. In larger surfaces showing oozing of blood, the same current may be used. Increase in the strength and holding of the electrode at a slight distance from the tissue causing sparking to the tissue will result in sealing by surface coagulation. In case of more profuse bleeding, the blunt coagulating electrode or hemostat should be used as already referred to.

In our series of 130 cases of intrapleural pneumolysis, we have encountered three profuse hemorrhages. The first was encountered early in our experience. It occurred during a clinical demonstration of the cutting of adhesions with the galvanocautery, according to the method of Jacobaeus-Unverricht. The patient was unfit for such a demonstration as the operation was difficult, because there were many adhesions to be cut. Frequent interruption, caused by letting others view the work through the thoracoscope, markedly delayed the operation, which was being done cautiously with only a minimum heat in the cautery because of vascular adhesions. The patient's state of mind, as a result of conversation, made it necessary to speed up the work, whereupon the heat in the cautery was increased to a moderate cherry-red glow. All went well for a short time, when suddenly a gush of blood smeared the lens, obstructing all view. The thoracoscope was quickly withdrawn and wiped clean, but on reintroduction, the lens at once again became covered with blood. Knowing the exact site of the bleeding vessel, we were able to change the patient's position on the table so that blood no longer fouled the lens and the bleeding vessel could be clearly seen. The hemorrhage was eventually controlled by cauterizing tissue immediately surrounding the vessel and also by touching the vessel itself with the tip of the cautery. Two liters of blood were aspirated from the pneumothorax three days later. The patient suffered no inconvenience as a result of the accident, but the harrowing experience is yet so vivid in

the mind of the operator that he is convinced that this type of operation is not appropriate for clinical demonstration to groups. Demonstrations should be confined to a selected, interested few.

Two other hemorrhages occurred in our recent series, and while profuse for a moment, they were easily controlled by electrocoagulation.

In case 6557, a woman, aged 25, referred for pneumolysis, had been under pneumothorax treatment for nine months. Stereoscopic films showed an uncollapsed cavity in the upper lobe of the right lung suspended by a cord adhesion attached to the anterior end of the third rib and by two string and one band adhesion attached between the second and fourth ribs posteriorly in the costovertebral gutter.

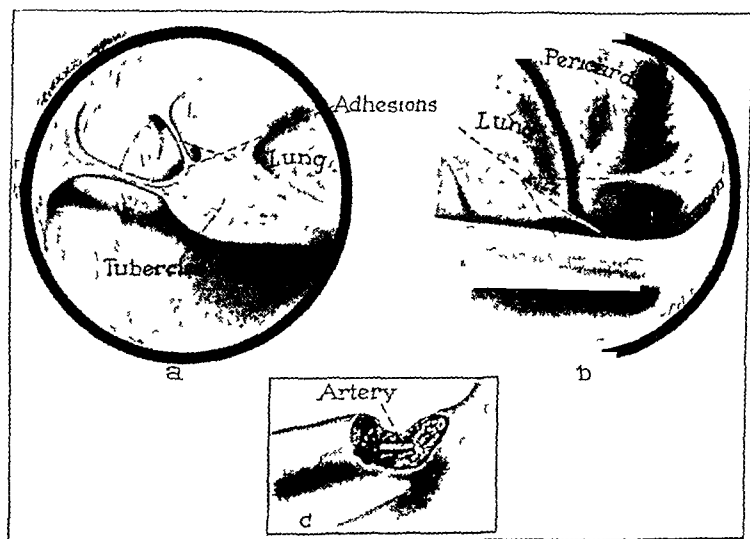


Fig 2 (case 6557)—*a*, thoracoscopic view of cord and band adhesions attaching apex of the lung to costovertebral gutter, *b*, view of cord adhesion attached to anterior end of fourth rib, also adhesions between pericardium and chest wall and small string adhesions extending from the lung to the anterior chest wall and *c*, partially cut cord adhesion (shown in *b*) attached to the anterior end of fourth rib, showing site of blood vessel

Thoracoscopic examination (fig. 2) confirmed these observations. The posterior adhesions were cut with the operating electrode after electrocoagulation and without anything unusual happening, as was expected. The cord adhesion anteriorly was then carefully studied. It was round, approximately 1 cm. in diameter (a minor affair from the standpoint of size alone). There were no blood vessels visible on its surface. It was densely organized and sensitive up to 3 cm. from the chest wall when all sensation disappeared. On slight coughing or clearing of the throat on the part of the patient, the adhesion increased

in diameter up to approximately 4 cm. from the chest wall, suggesting that it contained either the prolongation of a cavity or lung tissue, the former being suggested by previous stereoscopic film study. Pulsation of an expanding type was noted at the attachment of the adhesion to the chest wall, but not beyond 1 cm. from the chest wall. The pulsation was synchronous with the cardiac systole and not transmitted from the moving lung. A zone of electrocoagulation was made around the adhesion 2.5 cm. from the chest wall so as to avoid lung tissue and get as far away as possible from the chest wall.

The adhesion proved to be densely organized on cutting. Little contraction of the cut surface took place. Small blood channels were encountered as the cutting proceeded, which was always preceded by

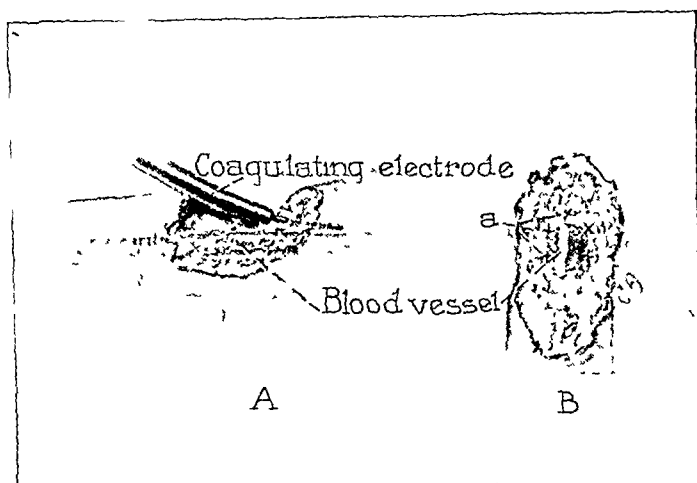


Fig 3 (case 6557).—A, pointed electrode in position for deep coagulation of blood vessel and B, blood vessel for deep coagulation showing site of punctures (a).

electrocoagulation. Suddenly, near the center of the adhesion, a blood vessel was cut into which had not been obliterated by the electrocoagulation, no doubt because of the density of the tissue and because the electrocoagulation current was not sufficiently intense. A stream of blood was projected across the pneumothorax cavity to the lateral thoracic wall. The lens, fortunately, was so placed that it did not become smeared with blood. The author's blunt electrode was placed on the bleeding vessel. But electrocoagulation at this point only made matters worse as the bleeding became more profuse, whereupon the pointed electrode was introduced into the tissue close to the wall of the vessel and the coagulating current increased for depth; this controlled bleeding immediately (fig. 3). The adhesion was cut through without further loss of blood. The patient suffered no unfavorable result from the

bleeding. Two hundred and fifty cubic centimeters of blood was aspirated from the pneumothorax the following day. The operation was a complete clinical success.

I am certain that the hemorrhage in this case would have been a serious matter if we had been obliged to rely on the galvanocautery for control. As a matter of fact, I do not think we would have attempted cutting this adhesion with a galvanocautery.

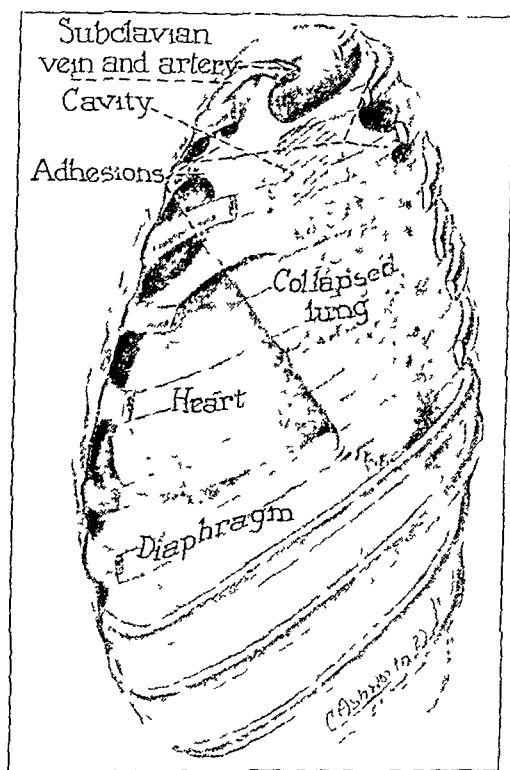


Fig 4 (case 6500) —Diagram showing distribution of adhesions between partially collapsed lung and chest wall as revealed by thorascopic examination

In the third case, no. 6500, a woman, aged 24, referred for pneumolysis, had been under pneumothorax treatment for ten months. At first, the quantity of sputum became diminished and then remained stationary, averaging from 40 to 60 cc. in twenty-four hours during the last two months of pneumothorax treatment, when she also developed tuberculosis of the larynx and extension of disease to the opposite lung.

Stereoscopic films showed a large cavity in the upper lobe of the left lung. There were many band and cord adhesions attached posteriorly in the costovertebral gutter and to the dome of the pneumothorax cavity

above the first rib. There were several cord and band adhesions attached to the anterior end of the first, second and fourth ribs.

Thoracoscopic examination revealed conditions shown in figure 4. All of the adhesions were densely organized and contained numerous sub-pleural blood vessels. At the first operation, a large band adhesion attached to the anterior end of the fourth rib, as well as a band adhesion holding the lung to the aorta (fig. 5), and two string adhesions at the apex were cut. One of the latter was attached to the wall of the subclavian artery, while the other was attached 4 mm. from the vessel (fig. 6a). No bleeding occurred, hemostasis being perfectly controlled by electrocoagulation; and no reaction followed the operation.

At the second operation, two large band adhesions, one attached to the first intercostal space (fig. 6b) and the second to the third rib in

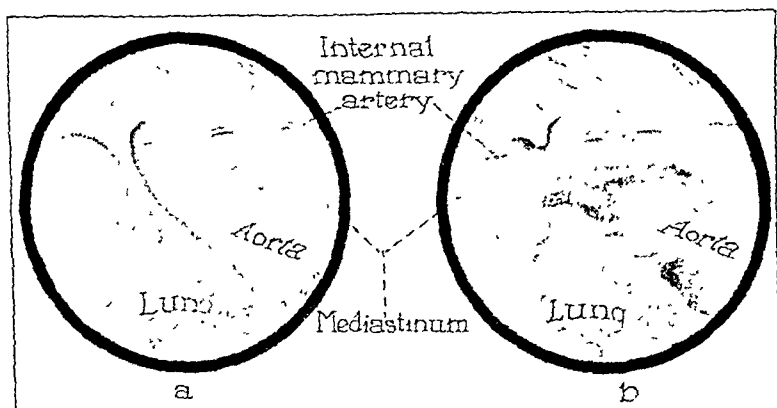


Fig. 5 (case 6500).—*a*, thoracoscopic view of band adhesion attached to anterior portion of second rib; *b*, view of same after cutting adhesion, showing band attached to the aorta.

the costovertebral gutter, were cut, again without bleeding or unfavorable complications.

At the third operation, two dense cord adhesions attached to the anterior end of the first and second ribs were cut. All of these operations were technically difficult, but bleeding was perfectly controlled by electrocoagulation, which alternated with the cutting. Following the operations, each of which was done at intervals of two weeks, an improved collapse of the lung was noted on stereoscopic films after each operation. The quantity of the patient's sputum was gradually reduced to 15 cc. as shown by daily measurement.

At the time of the previous operations, thoracoscopic study of the remaining adhesion showed that it was attached to the dome of the pneumothorax approximately 1 cm. distant from the subclavian artery just before this vessel crossed over the first rib. Furthermore, collateral

blood supply was seen emerging from beneath the subclavian artery and entering the base of the adhesion near its center. This collateral blood supply probably came from the *arteria cervicalis profunda*, which in this case may have been a branch of the subclavian artery instead of the costocervical trunk (fig. 7a). The adhesion was admittedly of a dangerous type, one we would not have considered cutting with the galvanocautery. Our success with electrosurgery, however, encouraged us to attempt it by the latter method, as the quantity of the patient's sputum had remained stationary at 15 cc. daily, and both stereoscopic film study and thoracoscopic study showed the remaining adhesion to be of great technical importance. Undoubtedly a satisfactory collapse of the lung (on which the patient's recovery depended) would not be obtained until it was severed.

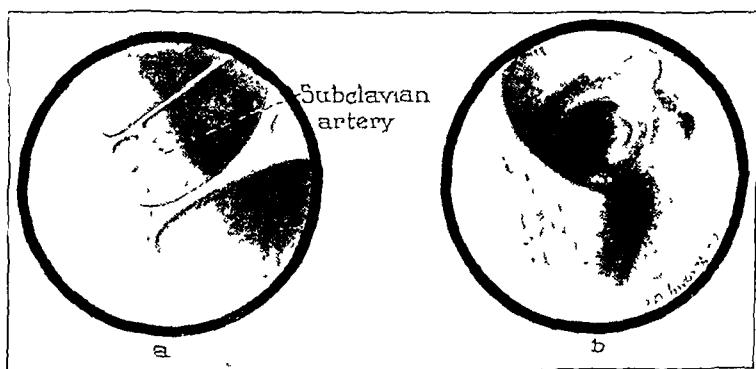


Fig. 6 (case 6500).—*a*, thoracoscopic view of two string adhesions extending from apex of the lung to the dome of the pneumothorax. One is attached to the parietal pleura covering the subclavian artery and the other is attached 4 mm. from the vessel; *b*, band adhesion shown in roentgenogram after cutting with endotherm.

The band was therefore carefully electrocoagulated on its outer surface, but because of its position, it was impossible to study its inner surface or put an electrode in a position to do an electrocoagulation of that surface. A line of electrocoagulation was made 2 cm. from the chest wall on the outer surface, and cutting followed with the undamped current, of moderate intensity, first, from the posterior edge toward the center and then from the anterior edge toward the center. As the center of the adhesion was approached from either side, the band was found to be more and more densely organized with tough bands of fibrous tissue between which were numerous blood channels. Owing to the dense character of the tissue, little retraction of the cut surface took place, and it was constantly necessary to resort to the coagulating current to control bleeding. On further approaching the site of the collateral blood supply.

after cutting through a particularly dense band of fibrous tissue, a sudden profuse hemorrhage took place. For a time it seemed uncontrollable, and preparations were made for blood transfusion and thoracotomy for the purpose of placing a clamp directly on the bleeding vessel. Fortunately, just at the moment when failure to control bleeding seemed imminent and no further time was to be wasted by attempting to control it with electrocoagulation currents, the method of puncturing around the blood vessel and doing a deep coagulation proved successful, and all bleeding stopped.

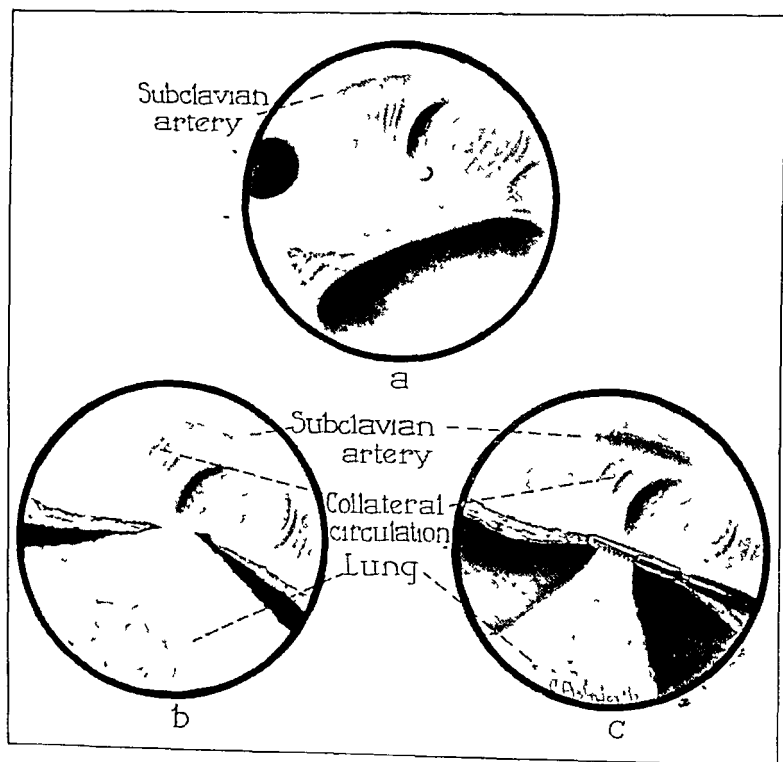


Fig. 7 (case 6500) —a, thoracoscopic view of apical adhesion, b, same adhesion partially cut; c, intrathoracic hemostat clamped on vascular remains of adhesion for purpose of electrocoagulation before cutting

It seemed reasonably certain that the vessel had not been severed but only cut into, and that the remaining portion of adhesion contained other blood vessels of a dangerous size. Lack of confidence in being able to control bleeding prompted us not to attempt further operation, at least until some more certain method of hemostasis could be developed.

The patient suffered no unfavorable symptoms as a result of the hemorrhage, except a slight febrile reaction which lasted three days. The pneumothorax cavity was filled with carbon dioxide gas, and the intra-

pleural pressure was considerably increased over former inflations. Forty-eight hours after operation, 400 cc. of bloody exudate was aspirated.

The quantity of the patient's sputum remained unchanged by the operation, as was expected, and for four weeks following operation, the daily quantity of sputum remained 15 cc. Anticipating such a course and convinced that a method must be found for cutting the offending band without danger of hemorrhage, I devised an intrathoracic hemostat which

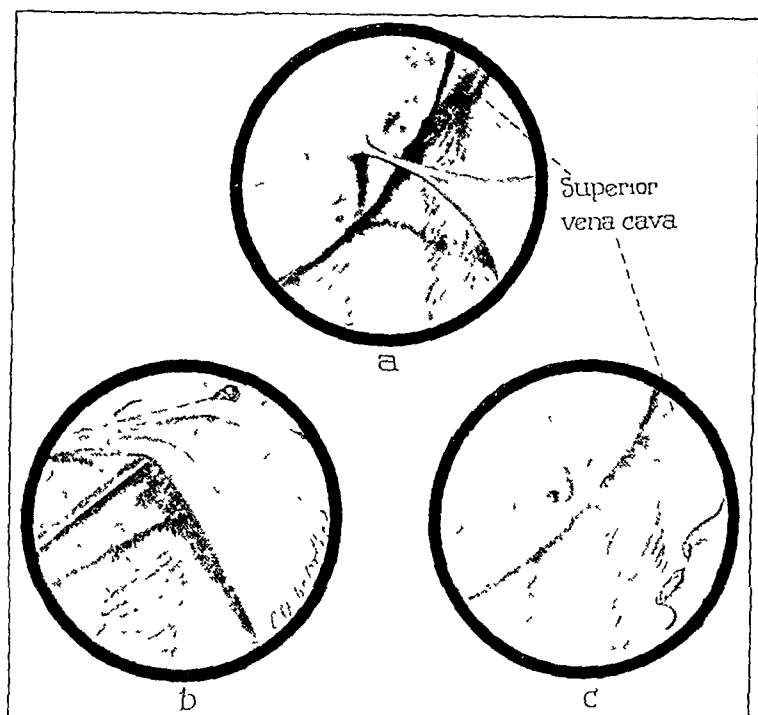


Fig. 8 (case 6172).—*a*, thoracoscopic view of a string adhesion, 5 mm. wide extending from the upper lobe of the right lung near the interlobar fissure to the lateral chest wall; *b*, method of examining structure of adhesion with author's blunt electrode; *c*, view of adhesion after cutting showing retraction of stumps.

was insulated so as to throw the coagulating current to the jaws of the hemostat. After the instrument was tested with satisfactory results, the final operation was decided on.

The thoracoscope was introduced in the first intercostal space mid-clavicular line. A superb view of the remaining uncut band was seen (fig. 7*b*). The collateral blood supply was seen as on previous examination. The adhesion had every indication of extreme vascularity. There was no necrosis at the site of previous cutting, and the cut surface was

clean. The intrathoracic hemostat was introduced in the third intercostal space midaxillary line and its jaws clamped down on the remaining portion of the adhesion which was then thoroughly electrocoagulated (fig. 7c). Cutting was then carried out without any loss of blood, no further electrocoagulation being necessary. Complete collapse of the lung followed.

The quantity of the patient's sputum promptly diminished, so that after two weeks the daily quantity ranged from 0 to 3 cc. During the course of these operations, a progressive improvement also took place in the opposite lung and larynx.

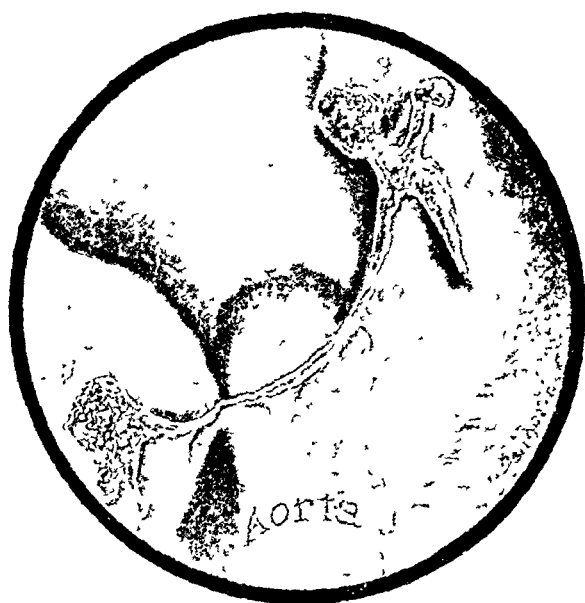


Fig. 9 (case 6489) —Thoracoscopic view of adhesion attached to anterior mesial aspects of chest wall and mediastinum and reflected over the aorta, after having been almost completely cut through

The danger of thrombosis of the vessel from heat of the galvanocautery and inflammatory reactions, as well as sloughing of tissue, has been pointed out in connection with cutting adhesions situated close to large blood vessels. In numerous cases, we have cut adhesions so situated which would not have been attempted with the galvanocautery. The following cases illustrate the value of electrosurgery in such cases.

In figure 8 (case 6172) is shown a thoracoscopic view of the apex of the right lung showing a fan-shaped adhesion extending from the apex of the lung to just above the sternal end of the first rib. The superior vena cava was 2.5 cm. distant from the point where the adhesion should be cut. In this case, some sudden unexpected movement

or coughing paroxysm on the part of the patient could easily have resulted in damage with a heated galvanocautery so close to a large blood vessel, for in spite of shutting off the current at the time the unexpected act was committed, the cautery could still remain sufficiently hot to do damage, whereas with the endotherm the instant the current is off, it is inactive and incapable of doing damage.

Figure 9 (case 6489) shows a thoracoscopic view of a dense band adhesion with its base attached to the anterior mesial aspects of the pneumothorax cavity and reflected over the aorta to which it was attached, showing cutting effected by the endotherm after electrocoagulation. This operation was executed without the loss of blood, and while extensive, it was not followed by inflammatory reaction on the part of the pleura. Complete collapse of the lung followed, and the patient's convalescence was uneventful.

In this case the operation was extremely difficult and prolonged, and without electrosurgery it would have been impossible to carry it out safely. It could not have been done with the galvanocautery except at a great risk.

COMMENT

1. Intrapleural pneumolysis is an operation of great utility. When it is properly done it is not dangerous and will convert a useless pneumothorax into an efficient one, thus saving the patient from thoracoplasty.

2. My experience with the electrosurgical method has given me confidence in this method of cutting adhesions. Control of bleeding is the most dangerous problem and requires thorough knowledge of the character of the currents used. Electrosurgical cutting is accomplished without heat or smoke to disturb the view. There is a minimum of tissue reaction afterward, and while more complicated and technically more difficult than the galvanocautery method, it is without doubt a notable advance in this branch of surgery, which is being more widely employed.

3. Intrapleural pneumolysis by the closed method is not a fool-proof procedure with either the galvanocautery or the electrothermic method. The operator must be familiar with the appearance of the pleural cavity and at all times perfectly orientated regarding the nature of tissue to be cut. This training in the use of the thoracoscope in the pleural cavity is just as important to the surgeon or phthisiotherapeutist as a thorough knowledge of the cystoscopic image is to the urological surgeon. The operator should have experience with pneumothorax and must have surgical training.

Acknowledgment is due Mrs. Henry F. Chaney, who, by a grant to the Portland Open Air Sanatorium, aided in this work.

THERAPEUTIC PULMONARY COLLAPSE

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AND

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With the exception of lobectomy, surgical intervention in the treatment for pulmonary tuberculosis and many other diseases of the lung has as its objective compression of the lung in part or as a whole. This is done, first, to rest the lung and aid the blood and lymph streams in handling the infection and thus to promote both absorption and scar tissue formation; second, for the obliteration of cavities, lessening infection, absorption and degenerative changes and also to eliminate the danger of hemorrhage through rupture of a blood vessel in a cavity; third, for the promotion of drainage by partial compression of cavities or bronchiectatic sacculations.

Every patient considered for pulmonary collapse must be studied carefully by both internist and surgeon, and a definite plan outlined. We believe all collapse to be selective, and that the judgment used in selection of patients, the type of collapse, time of operation and amount of compression will largely determine the results. Since we no longer believe that complete compression is necessary or even desirable, we attempt in all instances to determine the optimum therapeutic collapse.

For simplicity and convenience, we have divided our consideration of surgical collapse therapy into three distinct procedures. Artificial pneumothorax which includes the first and largest group of our cases will be considered as a surgical procedure, to differentiate collapse therapy from the usual medical routine.

PNEUMOTHORAX

Our experience with pneumothorax extends over a period of more than eleven years, while thoracoplasty, phrenicotomy, phrenic avulsion and other methods of surgical intervention were begun five years ago. We have experienced the usual successes, failures and complications. Patients with advanced disease have constituted the bulk of our failures with pneumothorax, and have furnished much of the material for phrenicectomy and thoracoplasty. Incidentally, with this group we have had the most complications, such as pleurisy with effusion, empyema, pleural shock and air embolus. During this period our patients have been grouped as follows: (1) patients referred from various sanatoriums for study and, when advisable, for surgical treatment; (2)

those seen in routine consultation of private practice; (3) patients from the municipal tuberculosis sanatorium at Richmond, and (4) patients admitted to the medical and surgical services of the Medical College of Virginia. Through these connections it has been our privilege to study a fairly large group.

In patients with moderately advanced pulmonary tuberculosis, pneumothorax has been used with favorable results and fewer complications. Many patients who are not responding satisfactorily to medical treatment improve rapidly when pneumothorax is instituted, and within a short time are able to return to their homes, resuming former occupations while continuing pneumothorax. We have grown bolder about the contralateral lung, not only with pneumothorax but with other surgical procedures. If the process in the contralateral lung is of the exudative type, we prefer to observe the patient until this has absorbed or fibrosis has taken place. Should the necessity for collapse seem sufficiently urgent, we sometimes institute pneumothorax even when there is a moderate amount of tuberculous infection of the exudative type in the contralateral lung. We are instituting pneumothorax earlier in the course of the disease and in a greater percentage of patients, and feel that in many with moderately advanced tuberculosis there is or has been an optimum time for pneumothorax therapy. When we encounter the patient with a hopelessly advanced condition pleading for an operation, we are convinced that many, if not most of them, were at some previous time suitable for pneumothorax, or other form of collapse therapy, probably when the disease was in the moderately advanced stage.

Tuberculous Pneumonia or Acute Exudative Tuberculosis.—In 1921, we first used pneumothorax in a patient with tuberculous pneumonia, the pneumonia following a profuse pulmonary hemorrhage. Prior to hemorrhage, this patient had a minimal tuberculosis. Pneumothorax was refused for control of bleeding, but consented to after the development of tuberculous pneumonia of the entire right lung. The lung was collapsed, and the patient recovered. Since then we have been collapsing the lung in these cases and using pneumothorax wherever possible in the acute exudative type of pulmonary tuberculosis. Of thirty patients with this acute type of process in whom pneumothorax was attempted, fourteen are apparently well and able to work; ten have partially recovered, and six have died. Of the ten who partially recovered, collapse was entirely satisfactory for five. Five developed fluid; three of these, tuberculous empyema. One patient with a bilateral process developed fluid, and later empyema. Thoracoplasty was done, and although the patient is still in a sanatorium, she is free from symptoms and the good lung has healed. Another patient who had the right lung collapsed for more than two years developed pneumonia throughout the left lung so that it

was necessary to withdraw air from the collapsed side and compress the pneumonic lung. Pneumothorax did not check the spread of tuberculosis in the pneumonic lung, and the patient had a spontaneous rupture followed by tuberculous empyema. By persisting with closed drainage,

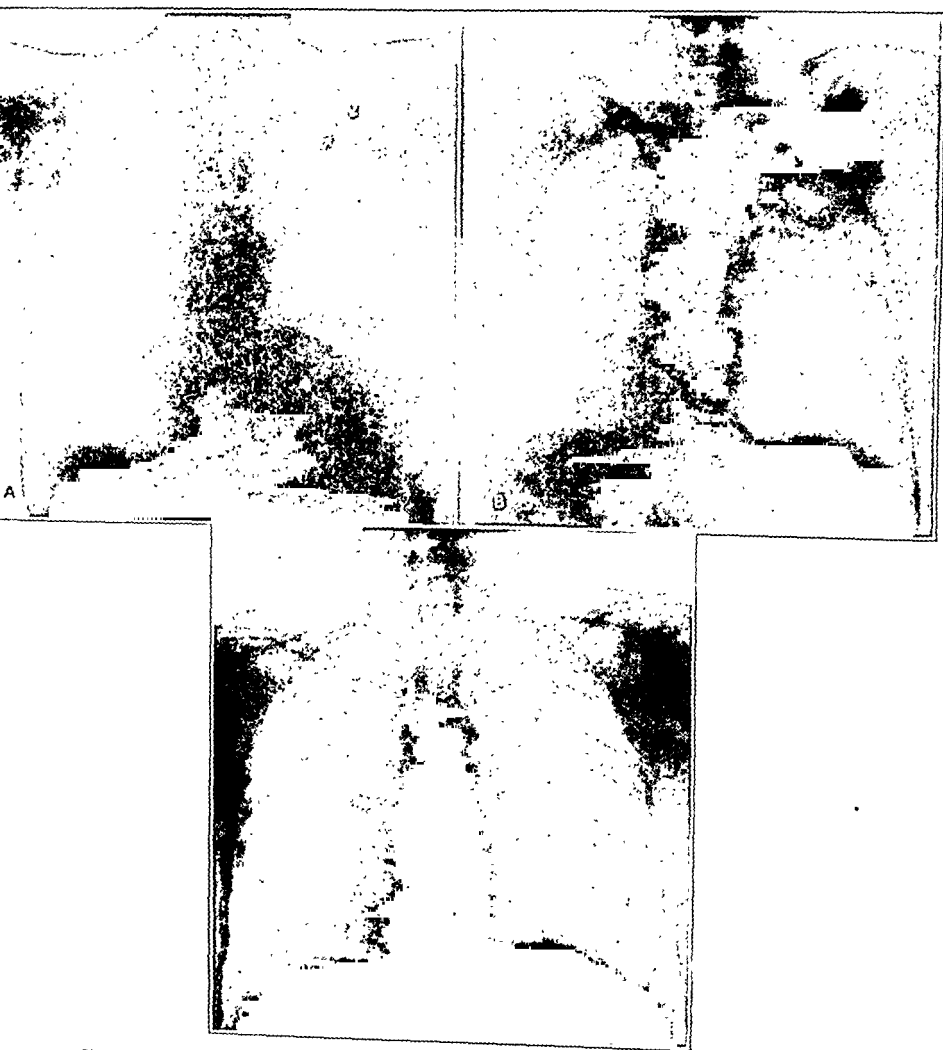


Fig. 1.—*A* shows acute peripheral abscess of the lung which has not responded to suitable forms of treatment; *B*, the lungs of the same patient after selective pneumothorax; *C*, reexpansion of the lung, just before pneumothorax was discontinued. The patient has remained clinically well.

we were able to clear up the empyema and later permitted the lung to reexpand. Multiple adhesions developed, including pleuropericardial and diaphragmatic, causing severe cardiorespiratory symptoms. Phrenic

avulsion was done giving immediate and complete symptomatic relief, but we believe that thoracoplasty will be necessary. In three patients with acute exudative tuberculosis, where collapse was ideal, the condition continued to spread and cavitate, and all the patients died.

Abscess of the Lung.—Fifteen patients with acute abscess of the lung have been successfully treated with pneumothorax. When this treatment was first begun we made the mistake of giving too much air, which hampered drainage and temporarily did harm. However, as soon as this was discovered sufficient air was aspirated to reestablish drainage, and the patients did well. Small quantities of air, never more than from 50 to 150 cc., should be given at frequent intervals, daily or on alternate days. There is no necessity or advantage in attempting to collapse the abscess cavity. A small amount of compression is sufficient to stimulate drainage and discourage further spread of the abscess.

We keep all patients with acute abscess of the lung at absolute rest in bed, using postural drainage several times daily. Bronchoscopies, vaccines and other measures are used as indicated. Nearly all acute abscesses of the lung will clear up when treated in this manner without the use of pneumothorax, but we find a few patients in whom pneumothorax is most helpful. One patient, treated with postural drainage and bronchoscopy, who was not responding, was given small injections of air daily with immediate improvement, becoming free from fever on the third day. No patient with a basal peripheral abscess of the lung has been given pneumothorax, but peripheral abscesses in the upper half of the lung have shown equally as good response as those in the hilar area.

We feel that pneumothorax is both unsatisfactory and unsafe in the treatment for chronic abscess of the lung. Two patients with chronic abscess died after pneumothorax, and in other patients treated in this manner results were unsatisfactory. We have abandoned the use of pneumothorax in such cases.

In the obliteration of empyema cavities or the collapsing of the chest for relief of symptoms from adhesions causing mediastinal or cardiac symptoms, or symptoms from pleural retraction or bleeding from excessive scar tissue formation, pneumothorax has no place, and other surgical procedures must be utilized.

Management of Patients on Whom Pneumothorax is Instituted.—Pneumothorax is instituted in the hospital or sanatorium and never at home unless in case of hemorrhage or other extreme emergency. All sick patients are kept at rest, and after pneumothorax they must remain in bed for a minimum of two months after becoming free from symptoms. Small quantities of air, from 100 to 300 cc., are given at frequent intervals with a small needle, from 20 to 23 gage, of necessary length.

A larger needle is never used unless fluid or pus is to be aspirated. When deflating a lung for the first time, sufficient warm physiologic solution of sodium chloride is used to separate the pleural surfaces. In this way injury to the visceral pleura is avoided, and a satisfactory manometer reading obtained without trauma. After pneumothorax, patients are followed up closely. Routine fluoroscopic examinations are done prior to every refill and roentgen examination made whenever indicated.

Complications we have encountered are empyema, pleural effusion, pleural shock and air embolus. We formerly had fluid to develop in approximately 50 per cent of all our patients after pneumothorax. In the last three or four years we have had less difficulty with fluid forma-

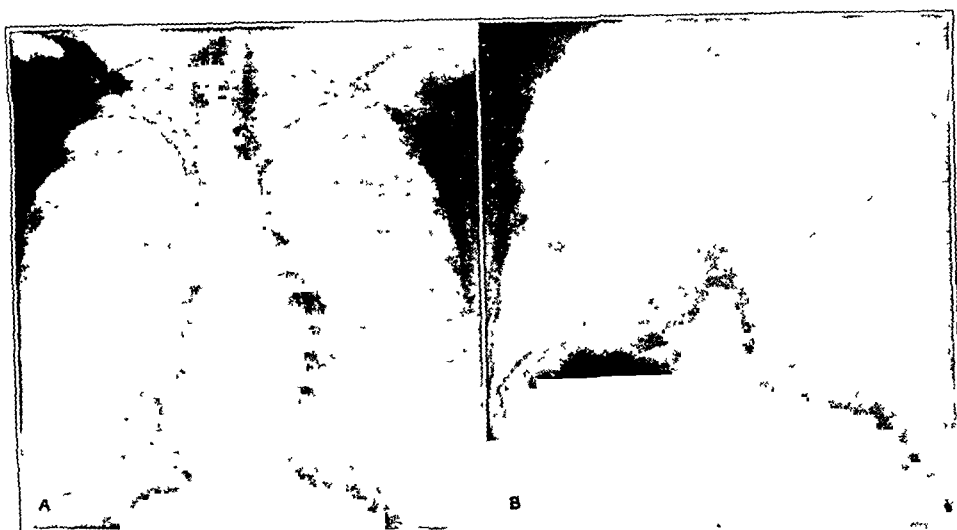


Fig. 2—A shows acute exudative tuberculosis. The sputum was loaded with tubercle bacilli and showed but few other organisms. B, taken after selective pneumothorax, shows basal collapse of tuberculous pneumonia on the right and mediastinal shifting producing partial compression of the pneumonic area at the base of the left lung.

tion, and now we encounter this in not more than 15 per cent of these cases. Empyema is a less frequent complication, but we believe that there is a small percentage of cases in which the development of empyema is inevitable. The better results in handling these complications and their less frequent occurrence we attribute to more careful selection of patients for pneumothorax; we are not using it as often in the patient with an advanced hopeless condition, thereby minimizing the stretching, tearing and other injuries here encountered. Small quantities of air are given at shorter intervals with less change of interpleural pressure, using a smaller needle, for less injury to the pleura. Patients developing effu-

sion after pneumothorax are put to bed, and, as in all cases of pleurisy with effusion, fluid is withdrawn and replaced by air. Should empyema develop, this is treated in the same manner using physiologic solution of sodium chloride and other irrigations. Thoracoplasty is not used in these cases until the more conservative measures have failed. On those patients who have not had previous treatment with pneumothorax, this is continued until fluid ceases to form. The lung is then permitted almost to reexpand, and from symptoms, physical signs, roentgen and fluoroscopic examination a decision is reached as to whether to continue with pneumothorax or permit the lung to reexpand. Pleural effusion has been attributed to calcium deficiency, salt retention, alkalosis, weak heart and low blood pressure, but we have been unable to see any direct relationship between these conditions and fluid formation. We believe infection, irritation and trauma to be the causative factors.

Symptoms attributed to pleural shock have been encountered in a number of instances, but are usually mild and promptly subside. In a few instances symptoms have been more severe. We have noticed that patients who suffer from pleural shock usually complain of pain even when the skin is being anesthetized. One patient with basal tuberculosis, treated with pneumothorax, complained of severe pain in the chest and neck the first time the needle was introduced. The pain grew worse with each succeeding deflation until pneumothorax was finally abandoned. At the last deflation, the patient was given a hypodermic injection of morphine and atropine to lessen the shock, but when the needle touched the parietal pleura, the patient screamed because of excruciating pain in the chest and neck. Both phrenic avulsion and thoracoplasty were done with the patient under ethylene anesthesia, and a normal reaction followed. Another patient with tuberculous pneumonia, on whom pneumothorax was started in September, 1926, received refills at regular intervals without pain or other evidence of reaction until the following December. After a refill of 200 cc. of air had been given the patient complained of symptoms which were attributed to mild pleural shock. At that time the patient had a uniform collapse of approximately 75 per cent without adhesions and otherwise entirely satisfactory. Symptoms subsided within a few minutes and the patient continued to be free from them until Jan. 25, 1927, when on the introduction of the pneumothorax needle, the patient screamed because of pain in the chest, shoulder and neck, and ceased to breathe. The needle had just reached the parietal pleura and no air had been given or even an attempt made to get a manometer reading. The patient's heart continued to beat regularly and otherwise normally under artificial respiration for thirty minutes, but we were never able to get her to breathe voluntarily, and she died in less than an hour. Autopsy was refused.

Air Embolus.—A patient with advanced tuberculosis and many adhesions was successfully treated with pneumothorax from May, 1926, to January, 1927. Following a refill of air on January 15, the patient suddenly complained of depression followed by a tingling sensation in the arms and hands, blindness coming on within a few seconds. The pulse became exceedingly slow, and the patient was unconscious in less than two minutes. The needle, having been withdrawn before the onset of symptoms, was reinserted and a marked negative manometer reading was noted, although pressure just previously was -2 . One hundred cubic centimeters of air was aspirated, and the patient recovered consciousness within a few hours, but sight and sensation did not return for



Fig 3—*A* shows tuberculous infiltration in both lungs and numerous cavities; *B* was taken three years after complete but selective thoracoplasty. Due to extensive involvement of the contralateral lung, more complete compression seemed then inadvisable.

twenty-four hours. One week later, during a refill of pneumothorax, the same symptoms occurred in a milder form. At this time, counting with the aid of a stethoscope, the heart rate was only seven beats per minute. Pneumothorax was abandoned.

Another patient, an old man with chronic abscess of the lung, suddenly died on the introduction of the needle. Respiration and the heart beat stopped almost simultaneously; we believe that death was due to cardiac failure and not to either air embolus or pleural shock. The accidents in these four patients are discussed somewhat in detail as we believe there is a difference in air embolus, pleural shock and cardiac failure, any of which may happen in pneumothorax treatment.

PHRENIC AVULSION

The second group in this study of surgical collapse consists of cases in which phrenic avulsion has been employed. Our series includes only eighteen cases of this type. But in reviewing even so small a series, certain phases regarding the use and value of surgical procedures on the phrenic nerve are worthy of emphasis. All of our cases of phrenic avulsion, with one exception, have been done under local anesthesia. We have attempted to remove from 6 to 10 cm. of the phrenic nerve; and have used both types of incision. In our first cases we followed the posterior border of the sternomastoid which gave a satisfactory exposure but a rather prominent scar. In the greater number of cases in the series an incision has been made about 3.5 cm. long just above and parallel to the clavicle. This has been found to give adequate exposure with a less noticeable scar. Granted a thorough knowledge of the anatomy in this region, little difficulty should be experienced during the procedure. It is fair to say, however, that this operation on an obese, short-necked patient will cause the surgeon a certain amount of mental anguish, while on a thin patient it will seem much easier. This, however, is true of all surgical conditions.

Reported injuries should be kept in mind. We have, fortunately, had no complication with the operation. The thoracic duct has never been exposed, nor has any damage to other structures been experienced. Infection of the wound has not occurred. A number of failures from operation on the phrenic nerve have been reported. Following carefully the work of Felex, we have made it a practice to note the size of the true phrenic nerve as each operation, and if there is any question about its size, we always make an effort to get the accessory phrenic as well. The anomaly is reported to occur in from 20 to 30 per cent of such cases. After phrenic avulsion, we have followed every case closely. Our first operation of this type was done five years ago. No patient has been made worse by the operation.

Clinical results supported by fluoroscopic studies have shown that our desired aim is attained by this operation. The diaphragm is paralyzed, with noticeable elevation, the latter depending on the present degree of adhesions. Beneficial results following this lesser procedure have been beyond our expectations, and we feel that it has a distinct and valuable place in one's armamentarium for therapeutic pulmonary collapse.

One of the most difficult conditions that comes into our clinic is bronchiectasis. Following the conservative school in a number of these cases, we have given relief by compressing the lung by means of phrenic avulsion, plus resection of the ribs. We realize that comparatively little support has been given the therapy of paralyzing the diaphragm as a treatment for bronchiectasis, and we wish to report favorable results in

selective cases by phrenic avulsion and postural drainage. Patients having a limited involvement closely associated with the diaphragm have shown distinct improvement, and many of them believe that they are well, although this optimism should not be overestimated. Clinically, they are markedly benefited. Any lesser operation which carries little hazard and offers improvement is worthy of consideration.

THORACOPLASTY

In the less fortunate patients with more extensive involvement, thoracoplasty in two or more stages, as advocated by Hedblom and others, has been our procedure. This type of operation may not produce a complete cure, but it has certain commendable features. The mortality of the operation is not a deterrent factor if it is carried out in stages.



Fig. 4—*A* shows advanced bilateral tuberculosis with a large apical cavity which grew larger in spite of the patient resting for months in bed. The remainder of the lung shows the tuberculous lesions mostly healed. *B* was taken after selective thoracoplasty with obliteration of the cavity. The patient is now clinically well and symptom-free

Every one of our patients of this type has shown improvement sufficient to justify return to previous occupation.

Pneumothorax has been tried in bronchiectasis with poor success. Since the advent of iodized oil and lung mapping, we have discontinued the use of pneumothorax in these cases even for diagnostic purposes.

Thoracoplasty as a means of producing pulmonary collapse in tuberculosis is a procedure well established in this body. Fifty-one patients with pulmonary tuberculosis have been subjected to this operation in our practice. A few were not given the complete standard procedure. In certain cases, a selective collapse was directed at the advanced pathologic process. Resection of the upper five ribs only was done on five of these



Fig 5—*A* shows basal râles, principally small and medium moist râles, at the left base posteriorly. A clinical diagnosis of bronchiectasis of the base of the left lung was made. *B*, taken following the introduction of iodized oil, shows bronchiectatic pockets just above the diaphragm, principally behind the heart shadow on the left. *C* was taken following phrenicectomy. The patient has had subsequent injections of iodized oil and has remained practically symptom-free. Her condition has been diagnosed as tuberculosis for nineteen years prior to our study.

patients, all of whom had additional involvement of the so-called "good lung." The first patient of this type was a poor risk, who was eager to take a chance for improvement. With some reluctance we resected the upper five ribs, expecting to complete the operation at a later period. Following the apical collapse, her condition improved so rapidly that she refused to have the complete operation.

No ill effects have followed this procedure. There has not been any extension of infection to the lower lobes, which has been reported as one of the contraindications to resecting the upper ribs first. On the other hand, it may be argued that an upper thoracoplasty is better borne by the patient than a resection of the lower ribs. In spite of the fact that resection of the first rib is the only difficult part of the operation, we feel that compression produced by apical collapse is the most important therapy, because it is directed at the root of the pathologic process. Furthermore, the better part of the lung is allowed to function and aid in expectoration. Resection of the lower ribs not infrequently causes cardiac embarrassment through its influence on the great vessels. The accumulated evidence seems to prove that resection of the upper ribs causes less reaction and is less hazardous to the patient. With our earlier cases in which we followed rather closely Sauerbruch's plan of operating, there was usually considerable reaction to the first stage of the operation, with a slighter reaction after the second stage. The disturbing post-operative course of these cases, plus the recommendation of Alexander, has influenced us to use phrenicotomy with an upper thoracoplasty. While this might not be suitable for all cases, especially if there is involvement of the lower lobe, we have had equally good results with a lesser amount of surgical intervention, which we believe to be sound reasoning.

SUMMARY

Briefly summarizing our conclusions from the foregoing fairly extensive study of therapeutic pulmonary collapse, we find that surgical collapse is rendered complete only by utilizing all our resources. These include: the carefully modified uses of artificial pneumothorax; phrenic avulsion and thoracoplasty, emphasizing the virtue of primary resection of the upper ribs. We believe that such selective collapse should receive foremost consideration. Careful choice of the type of collapse suitable for the individual case is of paramount importance, for no standard operation can be applied routinely to surgical pulmonary pathologic processes.

ABSTRACT OF DISCUSSION

ON PAPERS BY DRS. LILIENTHAL, WELLES, MATSON, AND COLE AND JOHNS

DR. EDWARD S. WELLES, Saranac Lake, N. Y. I should like to express my appreciation of Dr. Matson's paper, and I should like to add to Dr. Matson's argument for that procedure.

Five or six years ago, Dr. Jacobs came over to this country and demonstrated the method at several tuberculosis centers, but nobody seemed to like it. We did not take it up at Saranac Lake; the medical men there did not want it done. They were all afraid of hemorrhage as Dr. Matson says, because the view through the instrument was not sufficient to make the procedure safe.

About two years ago Dr. Matson came to Saranac Lake and demonstrated the same thing to us, except with the Unverricht instrument, and convinced all the phthisiologists of its value. They wanted me to use the operation; so I secured the outfit and have been doing it since.

I have used this procedure in from thirty to thirty-five cases now, nowhere near the number that Dr. Matson has, but a sufficient number of times to make me enthusiastic about it. I do not believe that it is being used enough throughout the country in the other tuberculosis centers. So far, I have had no bad luck with it. I have never had a serious hemorrhage, and of all the cases, I have had only one case of empyema.

I think that we are overlooking a valuable aid in the treatment for tuberculosis by not using this method because of possible imagined objections to it. It is difficult to do, and it takes a good deal of practice to be able to do it well, to localize oneself accurately in the chest and to learn how to handle the cautery with safety, but it can be done. It is not any harder to learn than cystoscopy, and I think that it is just as valuable in its field.

I think that Dr. Matson deserves a great deal of credit for the presentation of the subject.

DR. RALPH C. MATSON, Portland, Ore.: I regret that phthisiotherapists and thoracic surgeons in general do not appreciate to the extent justified the value of intrapleural pneumolysis by the closed method.

The phthisiotherapist is appreciating more and more the value of phrenic neurectomy and thoracoplasty and is more frequently referring these cases to the thoracic surgeon. The phthisiotherapist too often is guilty of continuing an unsatisfactory pneumothorax until the patient's condition is so hopelessly advanced that other operative measures cannot be utilized. This group of cases embraces about half of the pneumothorax group and therefore represents a large number of cases in which the patients could be benefited by other forms of collapse therapy, and one should especially consider an intrapleural pneumolysis first because if successfully carried out, the patient is spared from a thoracoplasty.

The phthisiotherapist needs education regarding the value of the entire group of surgical collapse procedures.

THE EFFECTS OF CLOSED PNEUMOTHORAX AND PHRENICOTOMY ON THE CARDIORESPIRATORY FUNCTION

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A considerable amount of work has been done on the physiology of various phases of respiration, and a great many interesting data have been collected concerning the circulation through the lungs in different stages of their expansion or collapse. Such data are valuable, but since in normal respiration the degree of distention or collapse of the lungs is constantly changing, the results of such experiments can only by inference be applied to the complete respiratory cycle.

However, from a therapeutic point of view, we are more concerned with the sum of the reactions of the cardiorespiratory mechanism as a whole throughout its complete cycles and in response to various strains put on it through pathologic changes or in the course of therapeutic procedures.

STUDIES ON THE CARDIORESPIRATORY MECHANISM

Consequently, it has seemed to us worth while to study some of the effects on the cardiorespiratory mechanism as a whole of certain conditions associated with pulmonary compression, and to try to discover something of the mechanisms whereby the body compensates for these effects. While primarily interested in the amount of blood flowing through the lungs per minute, we have included the study of certain other phases as well.

Dogs which had been completely anesthetized with rectal ether after a preliminary hypnotic dose of barbital (administered intraperitoneally) were used for these experiments. An animal was tracheotomized and connected with a spirometer filled with oxygen and containing soda lime to prevent increase of the carbon dioxide as the gas was rebreathed. The spirometer was so calibrated that it could be read accurately to within 5 cc. Experimental data obtained included pulse rate, respiratory rate,¹ the volume of the tidal air, oxygen consumption per minute, the oxygen content of the arterial and mixed venous blood, and in some instances the right and left intrapleural pressures. The oxygen consumption per minute was taken as the average reduction per minute in the volume of gas in the spirometer over a period of rebreathing of five minutes or more. Arterial blood was obtained by puncture of the femoral artery

1. The tidal air volume was taken to represent the depth of respiration.

and mixed venous blood, by direct puncture of the right side of the heart through the chest wall. The needle was introduced in the fourth right interspace close to the sternum to avoid puncture of the right pleura. Samples of blood were analyzed for their oxygen content by the technic of Van Slyke. The respiratory volume per minute was calculated from the tidal air volume and the respiratory rate, and the amount of blood flowing through the lungs per minute was obtained by dividing the oxygen consumption per minute by the difference

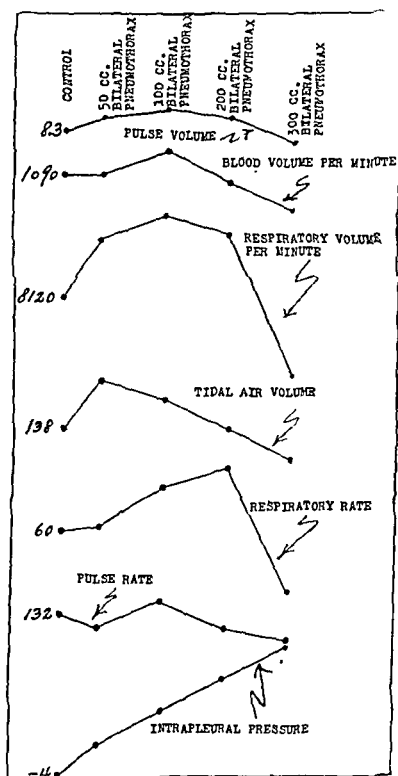


Chart 1.—Effect of increasing bilateral pneumothorax.

between the arterial and the venous oxygen contents. The pulse volume, of course, represents the blood flow per minute divided by the pulse rate. Practically no difference was noted between the effects of unilateral and bilateral pneumothorax of the same total amount.

The accompanying charts show typical experimental results. Chart 1 shows the effect of increasing bilateral pneumothorax in an animal weighing 10 Kg. Following the introduction of 50 cc. of air into each pleural cavity, the mean intrapleural negative pressure was decreased by 1 mm. of mercury. Coincident with this the tidal air volume was increased from 138 to 190 cc. (37.8 per cent) and the respiratory

volume, from 8,120 to 11,800 cc. per minute, or an increase of 45.3 per cent, largely due to deeper respiration. The amount of blood flowing through the lungs per minute was practically unchanged.

Bilateral pneumothorax of 100 cc. (200 cc. total) decreased the negative intrapleural pressure by one-half its normal value. The pulse rate was increased to 10 per cent above its initial rate, and the respiratory rate rose to 33 per cent above that at the beginning of the experiment. The tidal air volume began to fall, however, now being only 21 per cent above the first value, but due to the increased respiratory rate the total air breathed per minute was about 65 per cent above the initial amount, an increase of 5,260 cc.

The total amount of blood circulating through the lungs per minute now reached its maximum at 27 per cent above the resting value.

From this point onward, further increase in the pneumothoraces was followed by changes which may be interpreted as signs of beginning decompensation. Thus, bilateral pneumothoraces of 200 cc. (a total of 400 cc) reduced the mean intrapleural negative pressure still further to -1 mm. of mercury and caused a slowing of the pulse to 10 per cent below the rate at the outset. The respirations were increased to 90 per minute (+ 50 per cent) but were definitely labored, and even with the added effort they accomplished the inhalation of only the same amount inspired with the animal at rest before the beginning of the experiment. The respiratory volume per minute fell somewhat (10 per cent) from its peak, but due to the rapid respiratory rate it still remained 54 per cent above its initial value. This amount of pulmonary compression seemed definitely to interfere with the circulation through the lungs, for this was decreased by 31 per cent +, being now slightly below the resting value.

Bilateral pneumothoraces of 300 cc. each (600 cc. total) caused dangerous symptoms. The mean intrapleural pressure became practically 0, and the pulse rate had fallen to 25.3 per cent below the rate at the outset. Respirations became more labored and considerably slower (32 per minute, a decrease of 47 per cent), and the amount of air taken in with each inspiration fell to 25 per cent below the quantity at the beginning of the experiment (63 per cent below the peak). The respiratory volume per minute fell off sharply to about 60 per cent below its initial value (124 per cent below its peak). The circulation of blood through the lungs was also considerably interfered with and was reduced in amount to 26.5 per cent below its resting value (or 53.5 per cent below the maximum). The pulse volume was also decreased to 7 per cent below the initial value or 24 per cent below the maximum.

Thus, with an intact cardiorespiratory mechanism the body responds to the presence of closed pneumothorax by an increase in the pulse rate and pulse volume—after a slight initial slowing of the rate—

by an increase in respiratory rate, tidal air volume, and minute respiratory volume, and by increasing the amount of blood circulating through the lungs per minute. This compensation continues as the pneumothorax increases up to a certain point, which varies somewhat with the animal, but is followed by beginning failure of the cardiorespiratory mechanism as evidenced by sharp falls in all these factors.

The study was continued to include the effects of interference with certain other parts of the cardiorespiratory mechanism. The first of these studied was the effect of unilateral and bilateral paralysis of the diaphragm. Chart 2 shows a summary of these effects.

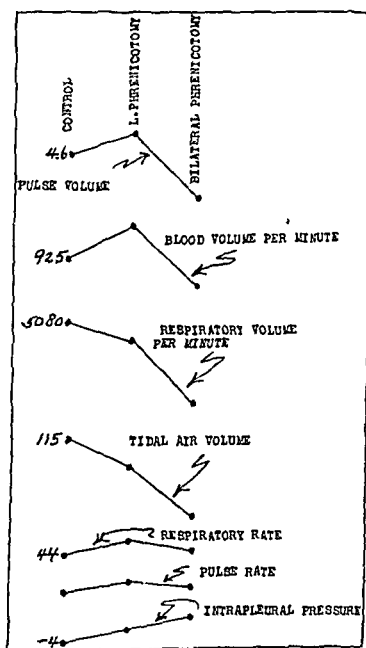


Chart 2.—Effect of phrenicotomy.

Unilateral phrenicotomy has been estimated to reduce the lung volume from one sixth to one third of its original value. Reference to the curves in chart 2 shows that in dogs paralysis of one half of the diaphragm produces effects quite comparable to those produced by a moderate pneumothorax. The mean negative intrapleural pressure is decreased somewhat, the pulse and respiratory rates are increased by about 10 per cent and the blood volume per minute is greater by 25 per cent than the resting amount. Because of the interference with the efficiency of inspiration, however, the tidal air volume and respiratory volume per minute are decreased by about 20 or 13 per cent, respectively.

So far, then, compensation has taken place, and indeed the pulmonary circulation seems definitely improved, as evidenced by the 25 per cent

increase in the blood flow per minute. Bilateral phrenicotomy, as would be expected, produces detrimental effects tending toward decompensation, and in this animal reduced the tidal air volume by 60 per cent, the respiratory volume per minute by 62 per cent and the quantity of blood flowing through the lungs per minute by 21 per cent, or to a point 45 per cent below that of unilateral phrenicotomy.

The reactions of an animal with unilateral diaphragmatic paralysis to pneumothorax are also of interest (chart 3). Whereas in the intact animal a pneumothorax of about 200 cc. produced an increase of the pulse rate, tidal air volume, respiratory volume per minute and the blood

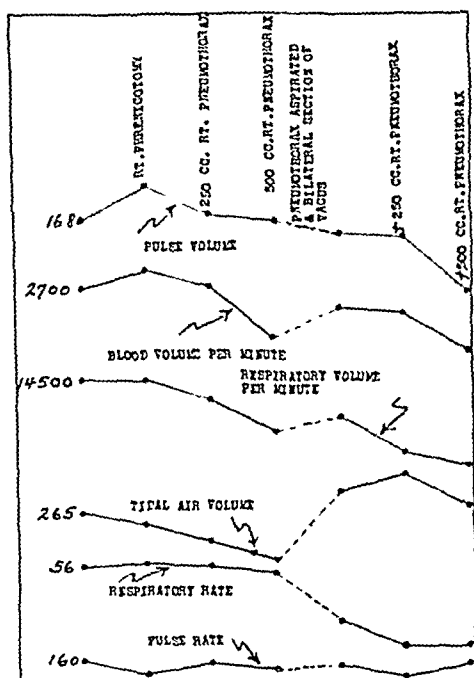


Chart 3.—Reactions of an animal with unilateral diaphragmatic paralysis to pneumothorax before and after bilateral section of the vagus.

flow per minute through the lungs, a similar pneumothorax when preceded by unilateral phrenicotomy causes a fall in all but the pulse rate, amounting in some instances to as much as 20 per cent of their previous values. Doubling the size of the pneumothorax produces grave symptoms of decompensation, as evidenced by reduction of the tidal air by 34 per cent, of the respiratory volume per minute by 39 per cent and of the blood flow per minute through the lungs by 38 per cent.

It is thus evident that the interference of such a factor with the depth of inspiration reduces the ability of the animal to compensate for an increased respiratory load.

The possible rôle of the vagus fibers to the lungs in the initiation of these compensatory changes is uncertain, but the reactions of an animal with bilateral vagotomy to pneumothorax are also interesting (chart 4).

Sectioning of the vagus nerves on both sides caused a slight increase in the pulse rate and slowed the respirations to one half of the previous rate. Coincident with this the depth of inspiration, as indicated by the tidal air volume, rose 150 per cent, and the respiratory volume

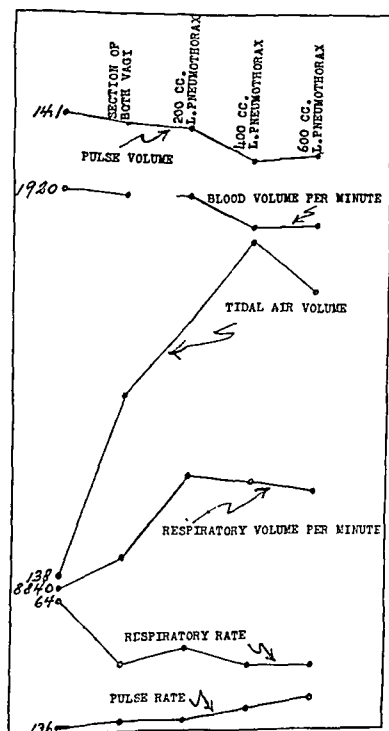


Chart 4.—Effect of unilateral pneumothorax after section of both vagi.

per minute was increased by 25 per cent. A slight decrease was noted in the blood flow per minute through the lungs (4 per cent) and in the pulse volume (9 per cent). A pneumothorax of 200 cc. here produced mixed effects. The respirations were slightly increased; the tidal air volume rose still higher, to 209 per cent above the amount before vagotomy was performed. As a result of this, the respiratory volume per minute was increased to 90 per cent above the initial amount. The quantity of blood circulating through the lungs per minute was slightly decreased, as contrasted with the 27 per cent increase in this factor produced by pneumothorax of equal size in the intact animal.

Doubling the size of the pneumothorax brought on signs of beginning decompensation and, except for an additional rise in the tidal air volume to + 270 per cent and a 12 per cent increase in the pulse rate, caused a sharp fall in all other factors measured. The amount of blood flowing through the lungs per minute was particularly affected, falling to almost 30 per cent below its initial value.

SUMMARY

1. A dog with an intact cardiorespiratory mechanism responds to a closed pneumothorax of moderate size by a slight increase in the pulse rate (10 per cent), a moderate increase in the respiratory rate (33 per cent) and tidal air volume (20 per cent) and a considerable increase in the respiratory volume per minute (65 per cent). In addition, the amount of blood circulating through the lungs per minute is increased by about 25 per cent and the pulse volume by about 15 per cent. Pneumothorax of a larger size causes symptoms of beginning decompensation, as evidenced by a fall in all these factors.

2. Unilateral phrenicotomy produces results similar to those produced by moderate pneumothorax, i. e., an increase of about 10 per cent in the pulse and respiratory rates, a moderate increase (about 25 per cent) in the amount of blood flowing through the lungs per minute, and an increase of about 15 per cent in the pulse volume. The tidal air volume and respiratory volume per minute are decreased by about 20 and 15 per cent, respectively, following hemiparalysis of the diaphragm.

3. Bilateral phrenicotomy produces symptoms of beginning respiratory decompensation in the dog.

4. A dog with unilateral phrenicotomy has a definitely decreased tolerance to further pulmonary compression, as evidenced by the fact that symptoms of beginning cardiorespiratory decompensation are produced by pneumothorax of a smaller size than is the case in an animal without hemiparalysis of the diaphragm.

5. Bilateral vagotomy causes a marked slowing of the respiratory rate (50 per cent) and an increase in the tidal air volume of 150 per cent and in the minute respiratory volume of 25 per cent. There is a slight decrease in the amount of blood flowing through the lungs per minute (5 per cent) and in the pulse volume (9 per cent).

6. Tolerance to pulmonary compression is also decreased following section of both vagus nerves.

ABSTRACT OF DISCUSSION

DR. E. A. GRAHAM, St. Louis: I should like to ask Dr. Andrus a question. I heard him say nothing about the amplitude of respiration.

DR. W. DEW. ANDRUS: Tidal air volume.

DR. GRAHAM: That answers it.

FUNCTIONAL ASPECTS OF BRONCHIAL MUSCLE AND ELASTIC TISSUE *

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LONDON, CANADA

Few medical practitioners will be found who do not know that the bronchial tree contains smooth muscle, but probably not many realize that this muscle forms a motor organ extending uninterruptedly from the larynx to the outermost terminations of the air-carrying tubes, and infiltrating the entire lung substance. Indeed, on account of the thickness and uniformity of its distribution, one recent worker, Baltisberger,¹ has averred that hardly a cubic millimeter of lung substance in the human being could be found which would not contain smooth muscle. There are reasons why the presence of this abundance of pulmonary muscle has not been observed earlier. One undoubtedly is the fact that in ordinary microscopic sections of the lung so much space is occupied by air that the tissues are spread apart, and the muscle elements, thus dispersed, do not bulk so large as they would if all the air could be eliminated and the muscle specifically stained. In such a case one would be struck at once with the relatively large amount of muscle present. Again, the muscle in the lung tissue occurs in delicate wisps, sometimes only a cell or two in thickness, and, since distinctive stains for muscle are seldom used, it does not contrast sufficiently with adjacent tissues to be appreciated.

ANATOMY OF THE BRONCHIAL MUSCULATURE

This muscle is not distributed in any haphazard fashion in the lung; on the contrary, it is built up in a characteristic and systematic manner. Most of it is in the walls of the airway, and is known as the bronchial musculature. This is by far the more important division. Some of the muscle, however, is scattered as slender strands and filaments in

* From the Department of Anatomy of the Faculty of Medicine of the University of Western Ontario.

* Credit for assistance in the preparation of this paper is gratefully acknowledged to the Marine Biological Laboratory, Woods Hole, Mass., where a work room and library facilities were placed at my disposal.

* This article is mainly a synopsis of a monograph entitled "The Musculature of the Bronchi and Lungs" which appeared in *Physiological Reviews*, vol. 9, no. 1, January, 1929. This contains a full bibliography. For a more thorough treatment of the different subjects, the original should be consulted.

1. Baltisberger, W.: Ueber die glatte Muskulatur der menschlichen Lunge, *Ztschr. f. Anat. u. Entwickl.* 61:249, 1921.

the interstitial tissue of the lung, and has, accordingly, been termed the interstitial musculature.

The bronchial musculature is found throughout the airway, and this means throughout the lung tissue. In the trachea it exists in the posterior, flaccid, membrane as thin transverse strands which tie together the ends of the cartilage crescents. Some fibers, particularly in the region of the carina, course obliquely, or longitudinally.

In the main bronchi there is much the same arrangement, the fasciculi of muscle, at first, bridging the interval between the cartilage ends; but soon, as the cartilages come to be distributed around the entire wall, the muscle also becomes a complete layer, lying as a delicate tubular network between the cartilages and the mucosa. The predominant course of the strands in the larger tubes is circular, and the elongated, transverse meshes vary in size and shape depending on the state of elongation or contraction of the tube. This netlike muscle tube is an integral part of the wall; there is no interruption in it, and it branches and rebranches with the air tubes, the caliber progressively becoming smaller and smaller. The area of the cross-section of the branches, however, always exceeds that of the parent trunk. The muscle, too, becomes actually more delicate as the tubes become smaller, but, when considered in relation to the bulk of the other constituents in the wall the muscle is more prominent. This is particularly true of the fine terminal bronchioles which mark the end of the purely conducting part of the airway, and lead over into the combined conducting and respiratory part. In the terminal bronchioles the muscle is relatively heavy, and is capable, apparently, of obliterating the lumen of the tube, on contraction (figs. 1 and 2).

The anatomy of the conducting part of the airway is familiar to every surgeon, and need not be discussed here. But when the terminals of the airway are considered—the conducting and respiratory portion—it is found that the anatomy is not usually so well known and, on this account, a short description will be given of this, more recently studied, division, as a preliminary to the consideration of the muscle in its walls.

The fine terminal bronchioles of the air system, corresponding to the finer arterioles of the blood system, are relatively narrow; indeed they are said to be the narrowest part of the airway. They branch into the respiratory bronchioles, so called because their walls are broken by openings leading into air-holding chambers, some of which are clothed by cuboidal epithelium; others are covered with such thin-walled epithelium as to make them capable of allowing gaseous interchange between the air and blood. As these respiratory bronchioles are traced outward, the openings become more numerous and larger. They branch into wider tubes, which are of characteristic appearance, and are called

alveolar ducts. These ducts are important air-carrying tubes. Their walls, if they can be called walls, are mere, large-meshed sieves, the rounded openings sometimes leading into branches like themselves, but more frequently into loculated alveolar sacs, which end blindly. These alveolar sacs, or air-sacs as they are often called, are often partially divided by low, crescentic partitions, into two or more chambers, which are known as alveoli. Thus the alveoli are mainly subdivisions of the

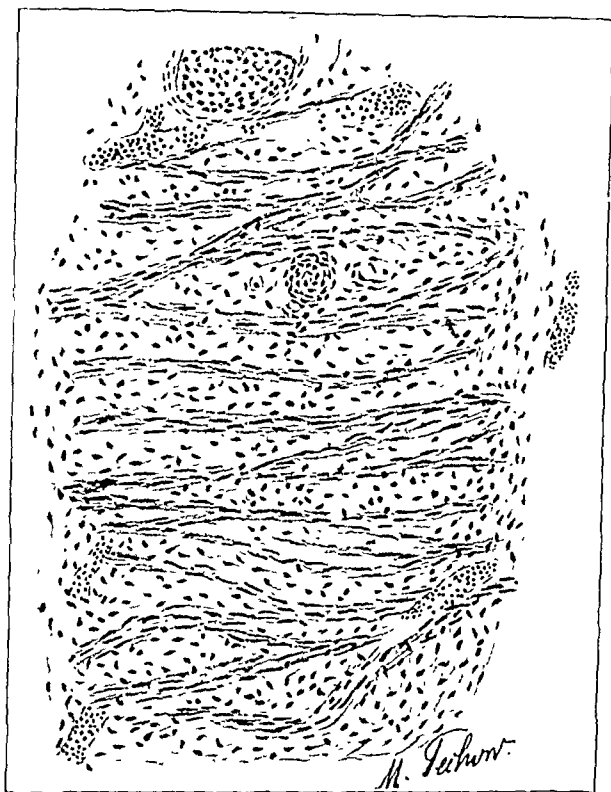


Fig. 1.—(From Eduard Müller, *Zur Anatomie der Bronchialmuskulatur*, Sitzungsber. d. Gesellsch. z. Beförderung d. ges. Naturwiss. z. Marburg, May, 1913, abb. 2.) Musculature in a bronchus of 0.8 mm. diameter from a new-born child.

alveolar sacs. Some, however, open directly from the alveolar ducts or respiratory bronchioli; in this case a unilocular alveolar sac and an alveolus would mean the same thing.

Thus the pulmonary lobule, or acinus, which is all that branched complex of air tubes, air chambers and their adnexa, the stem of which is the respiratory bronchiole, is complicated. It is only recently that its labyrinthine character has been visualized. The accompanying figure

of Willson² (fig. 3) will assist in giving some idea of this structure, or, more correctly, a small portion of it. A terminal bronchiole³ (1) is shown dividing into two respiratory bronchioles, each of which (2) again divides into two alveolar ducts. Only one of these (3) was followed by Willson,⁴ in his study, and this divided twice in rapid succession (4, 5). Only one of the latter branches⁵ (6) was traced to its ultimate terminals. These ramifications (7 to 26) were all pro-



Fig. 2.—(From William Snow Miller, *Am. Rev Tuberc* 5:693 (Nov.) 1921, fig. 2.) Muscle bands from bronchiolus from the lung of man

2. Willson, H. G.: The Terminals of the Human Bronchiole, *Am. J. Anat.* 30:267 (May 15) 1922; The Emphysematous Lung, *Univ. Toronto Med. Bull.* 8:9 (Dec.) 1927.

3. Macklin, C. C.: The Musculature of the Bronchi and Lungs, *Physiol. Rev.* 9:1 (Jan.) 1929.

4. Willson (footnote 2, first reference).

5. Kölliker, A.: *Mikroskopische Anatomie der Gewebelehre des Menschen*, 1852.

jected on a sheet of paper. On this branch and its ramifications alone one can count some seventy-one alveolar sacs of various sizes, to say nothing of the many small alveoli. Thus the number of respiratory chambers in a single pulmonary lobule must be enormous. Willson noted much variation in the size of the alveoli, and of the air sacs, and found many respiratory chambers which might with equal propriety be called either large alveoli or small air sacs.

In the lobule the essential happenings of external respiration—the gaseous interchanges between the air and the blood—go on. It must, therefore, be capable of being ventilated—of expanding and contracting.

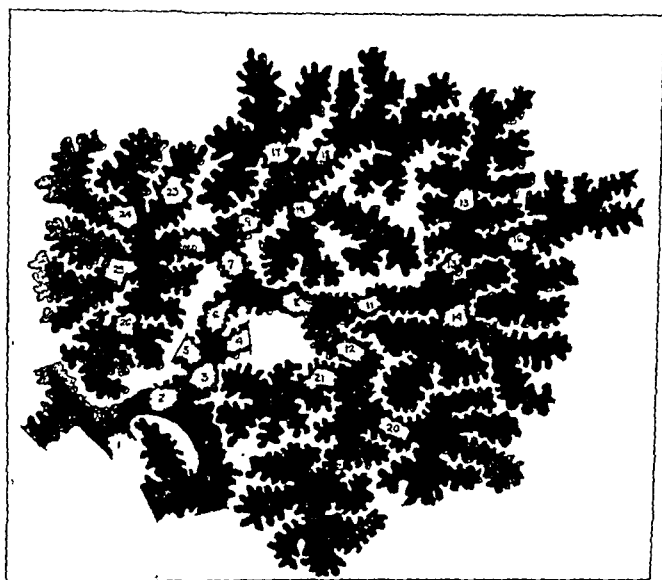


Fig. 3.—(From Willson, Herbert G., *The Emphysematous Lung*, Univ. Toronto Med. Bull. 8:11 (Dec.) 1927.) Diagram of some of the terminal ramifications of a nonrespiratory bronchiole of the lung of a child, projected on a single plane. All these branchings occur in a piece of lung about the size of a pinhead.

Indeed Keith⁶ has termed it, rather appropriately, the “bellows part” of the lung. To understand its action is to understand the mechanical action of the lung; and the muscle is an important, indeed an indispensable, element in it. I shall now return to a consideration of this muscle.

The network, mainly of circular fibers, passes directly on from the terminal bronchioles into the pair of respiratory bronchioles, and thence, without interruption, into the ultimate ramifications of the alveolar ducts, and some of its fibers even dip into the lining of the alveolar sacs.

6. Keith, A. *The Mechanism of Respiration in Man*, in Hill, L.: *Further Advances in Physiology*, London, Arnold, 1909.

In the respiratory bronchiole the muscle strands run obliquely, or, as Miller⁷ has aptly expressed it, in "geodesic lines." When openings occur in the walls the strands encircle these, but the muscle here, and everywhere, is to be regarded as part of the wall of the tube rather than as belonging to the outpouching. If such a tube is split open and laid flat, with the muscle appropriately stained, it would look as shown in figure 4, from Baltisberger.¹ The openings outlined with black lines lead into alveoli. Figure 5 shows the muscle as seen in

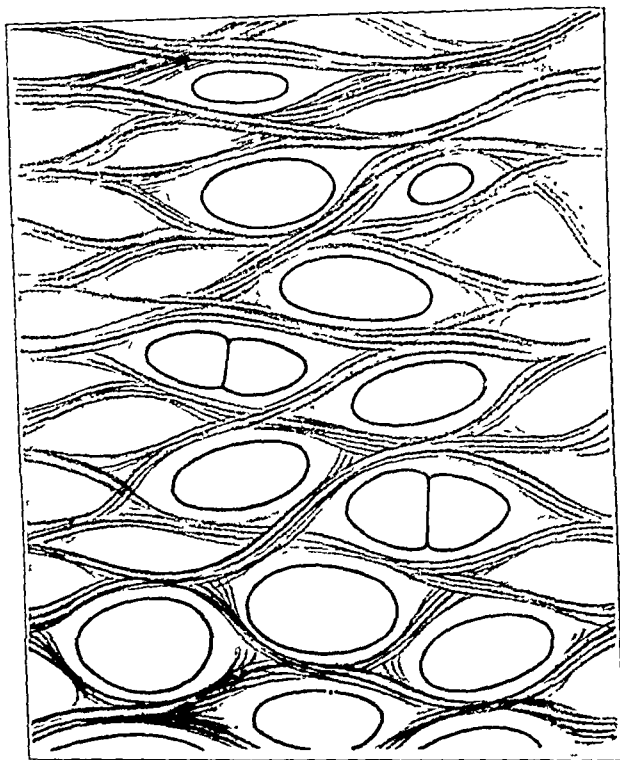


Fig. 4—(From Wilhelm Baltisberger, *Ztschr. f. Anat. u. Entwickl.* **61**:259, 1921, abb. 4.) Diagram of the wall of a respiratory bronchiole, in man, split lengthwise and laid flat. The longer, vertical axis is the axis of the tube. The cut was made along the line of contact of the pulmonary artery, where there are no alveolar outpouchings. In the central part of the field, opposite the artery, the alveoli are numerous, particularly in the lower part of the field, which is the most peripheral region.

longitudinal sections of this tube. It is cut transversely and is marked m_1 to m_4 , "a" is an alveolus lined with cuboidal epithelium; s_1 to s_3 indicate the walls between the alveoli.

7. Miller, W. S.: The Musculature of the Finer Divisions of the Bronchial Tree and Its Relation to Certain Pathologic Conditions, *Am. Rev. Tuberc.* **5**:689 (Nov.) 1921.

In the alveolar ducts, the meshes of the net become larger and larger, since so much of the essential wall is occupied by the openings into the offshoots already described. The muscle net of the wall of an alveolar duct, if split open and laid flat, would appear loose, with

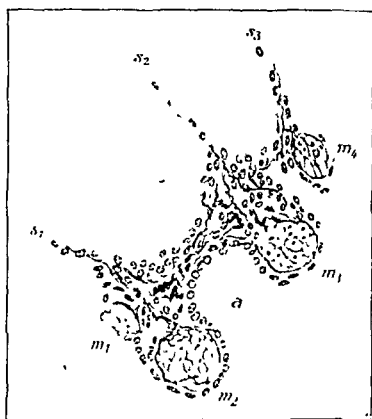


Fig. 5.—(From Baltisberger, abb. 2, p. 256.) Section from the wall of a respiratory bronchiole, in man, showing four muscle bundles, m_1 , m_2 , m_3 , and m_4 , cut transversely or obliquely; a is an alveolus, lined with cuboidal epithelium.

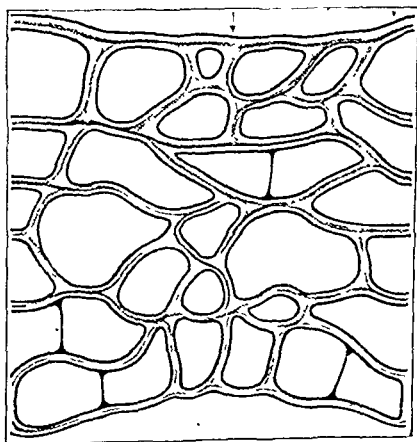


Fig. 6.—(From Baltisberger, abb. 9, p. 265.) Diagram of the wall of an alveolar duct, in man, which is represented as split lengthwise and laid flat. The vertical axis of the figure is the axis of the duct. The air sacs are outlined in black, and the muscle network is represented in gray.

delicate strands, as shown in figure 6, from Baltisberger. Strands from the muscle net of the alveolar ducts are often continued into the alveolar sacs. The larger sacs have a similar wall, but it is even more

delicate, and the muscle is lacking in many of the edges of partitions separating alveoli. In such cases the thin margin of the partition is made up only of delicate strands of white fibrous and yellow elastic tissue.

Reproductions of figures from Baltisberger's fine work are here given to make the meaning clearer, and to enable one to visualize the complicated structure of the terminal air ducts and chambers. In figure 7 is

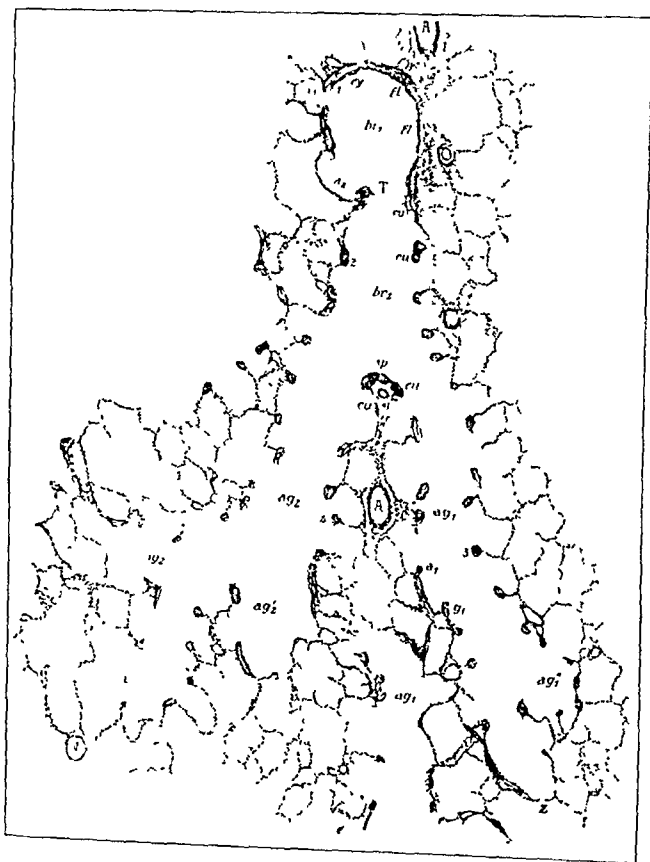


Fig. 7.—(From Baltisberger, *abb. 3*, p. 257.) Drawing of the branching of a respiratory bronchiole into two alveolar ducts in lung of man. The sections of the muscle bundles are represented in the dark nodules, apparently projecting into the ducts and attached by slender stalks. The latter really represent the interalveolar partitions. The muscle rings have been cut in many different directions.

shown a respiratory bronchiole br_1 cut directly across, in the upper, or apical, part of the picture. The openings in the wall are seen, leading into alveoli a_1 and a_2 . The muscle is cut almost directly longitudinally. The tube leads, at "T," into a branch like itself, br_2 , which branches into two alveolar ducts, ag_1 and ag_2 . All along the walls of these tubes

the cut muscle appears as small dark nodular structures of various sizes and shapes. Each nodule is connected outwardly with a thin partition, separating adjacent air chambers. For the most part, the muscle rings are cut directly across, or at a sharp angle, but some are cut tangentially, and appear as more elongated structures, in the figure. This is a favorable section, since the alveolar ducts are cut longitudinally. It is not always possible to secure them so cut. The nature of the alveolar sacs is well seen. One readily grasps how contraction of this tubular net would diminish the space within, and tend to force the air either laterally, into the air chambers, or forward, along the tube,

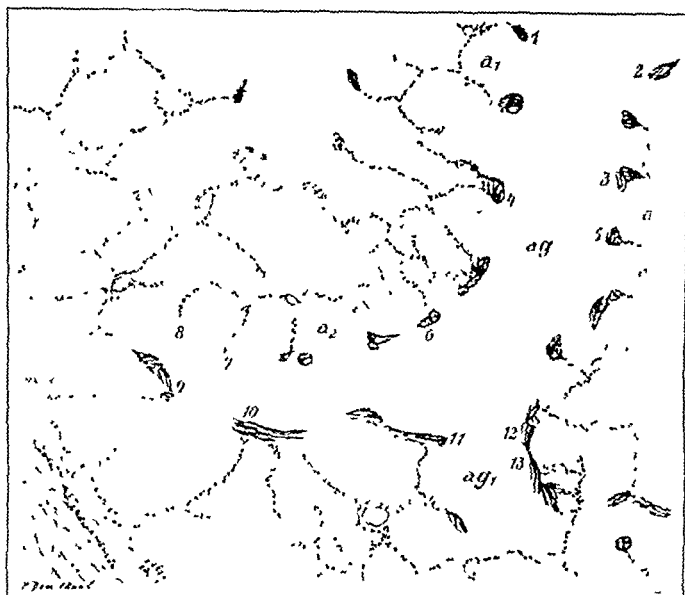


Fig 8—(From Baltisberger, abb 5, p 262) Drawing from a section cut longitudinally along an alveolar duct in a human being. The muscle bundles, shown as a double row of dark nodules, which line the lumen of the duct, have been cut in different directions. The muscle bundles have numbers, and the air sacs are marked a_1 , a_2 , etc., ag is the lumen of the alveolar duct.

toward the larger bronchi. The latter movement, of course, occurs in normal expiration, as this is the direction of least resistance.

Figure 8 shows, again, a longitudinal section along an alveolar duct, ag , at a somewhat higher magnification. The muscle lines the lumen of the tube, and is seen in the darker, stouter, structures. As before, the rings have been cut at various angles. If, instead of a thin section, one were looking into a slice of tissue which would show the far side of the tube, it would be seen that the muscle formed a network as described, and as shown spread out flat in figure 6.

In figure 9 is seen another thin section through an alveolar duct, showing the muscle grouped about the central lumen, marked *ag*. The muscle nodules are numbered 1 to 6, and each is but part of a circle. The elastic tissue infiltrating the muscle is not seen in these figures. In figure 10 is shown a tangential section along the wall of an alveolar duct which shows how these sphincteric muscle structures are woven together to form the wall. Figure 11 shows a section across an alveolar duct, *ag*, in which a complete circle of muscle is shown. Not many

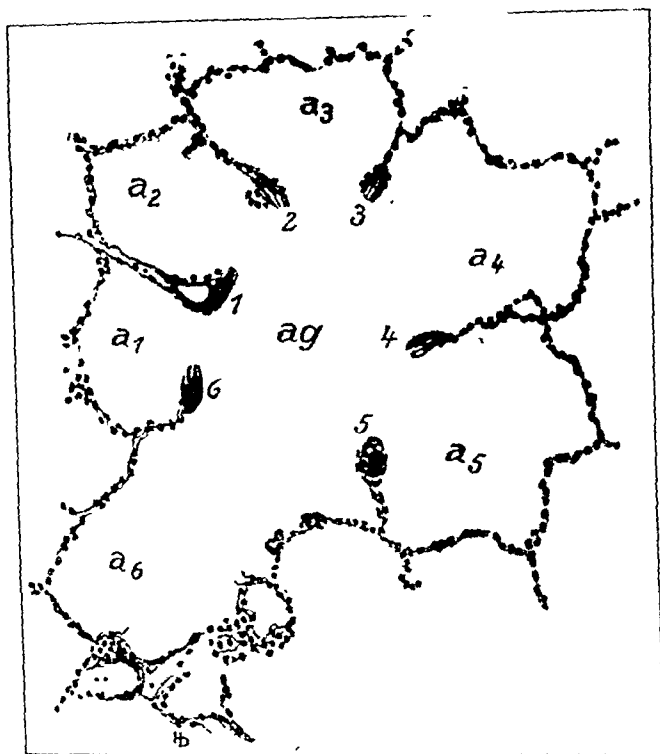


Fig. 9.—(From Baltisberger, *abb.* 6, p. 263.) Drawing showing a cross-section through an alveolar duct *ag* in a human being. The muscle bundles, cut for the most part transversely, bear numbers, and the air chambers bear the general designation *a*, and they show a typical rosette form.

such are seen in a field. Although no openings into outlying respiratory chambers appear in this section, they would come into view in adjacent sections, if these could be seen. Figure 12 is a photomicrograph of one of my own preparations from the lung of a cat, showing a somewhat similar muscle ring.

Nowhere is muscle found in the walls of the alveoli—only in the mouths of these—and not always there. It is always to be regarded as belonging to the tube or sac into which the alveolus opens, and never as part of the alveolar wall.

In the alveolar ducts and larger alveolar sacs the lining presents an appearance reminiscent of the lungs of the lower vertebrates, such as the frog. Indeed, it has long been known that the unit of the mammalian lung, including that of man, is built up like that of these lower animals; and Kölliker⁵ and others, many years ago, called attention to

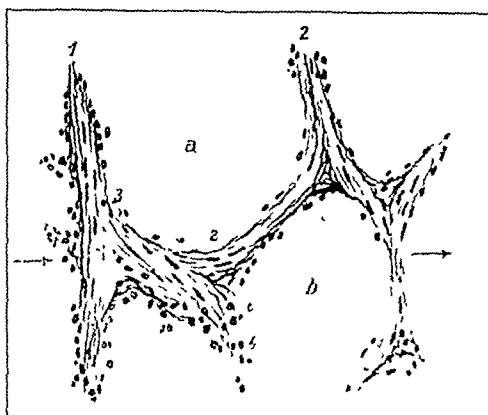


Fig. 10.—(From Baltisberger, abb 8, p. 264.) Tangential section along the edge of an alveolar duct in a human being, showing the way in which the muscle bundles interlace with one another. The arrow indicates the long axis of the duct. The numbers indicate muscle bundles running in different directions; a and b are openings into air chambers.

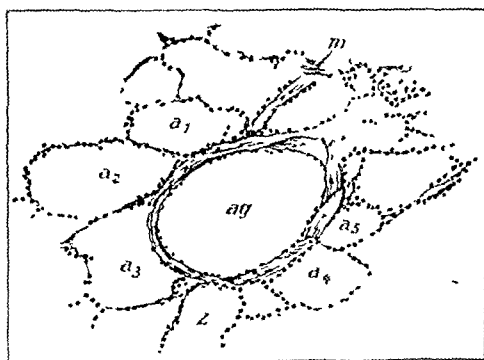


Fig. 11.—(From Baltisberger, abb. 7, p. 263.) Oblique section through an alveolar duct in a human being, cut through the muscle in such a way that a complete ring appears in the section. The muscle fibers in this ring, however, appear interwoven. ag marks the lumen of the duct.

this resemblance. Because of this similarity I am here showing the interior of a locus of the lung of the turtle (fig. 13). In structure it is essentially like the larger alveolar ducts of the lung in man, but is built with chambers of much greater size and much heavier parts. The lining

of the locus will be seen in the surface network in which, as in the mammalian lung, the muscle fasciculi are by far the most bulky constituent. A cross-section of one of these lining strands, stained to show the muscle, is presented in figure 14. The muscle is here much more dense than in the mammalian lung, as a comparison with figures 10, 11 and 12 will show, and the interalveolar partition joining it is considerably heavier, and has a capillary field on either side, but the general arrangement is the same.

Thus it is seen that whatever "wall" there is in the air tubes of the pulmonary acinus is made up of this muscle net with its infiltration

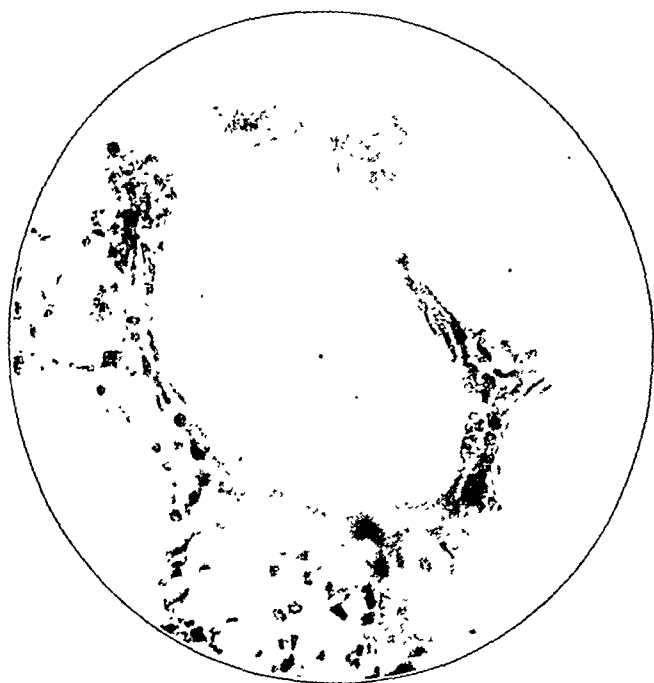


Fig. 12.—Photomicrograph from moderately inflated cat lung. The muscle ring does not lie quite in the optical plane. Compare with figure 17, showing elastic tissue in a similar region. Appearances of this kind are found everywhere in thick sections of this kind. (Author's preparation.)

of elastic tissue; for the covering of epithelium and tunica propria which this network bears is exceedingly thin. The wall is thus a tubular, branched, contractile, myo-elastic net. Of what use is it? Why is it there? An answer to this question will not be attempted until another important and closely related structure, the elastic-tissue structure of the bronchial tree, is described. This is so intimately interwoven with the muscle as almost to compel the term myo-elastic complex rather than either muscle or elastic tissue alone, for the two are functionally inseparable.

The Elastic Tree.—Like the arbor musculosa, the arbor elastica is found as a continuous system from the larynx to the alveoli, and, not stopping with the mouths of the final air chambers, as in the case of the muscle tree, it is continued on, as exceedingly delicate strands, into the alveolar walls.

In the larger tubes the elastic tissue is in several layers, which have been well described by James Miller.⁸ An illustration from this author

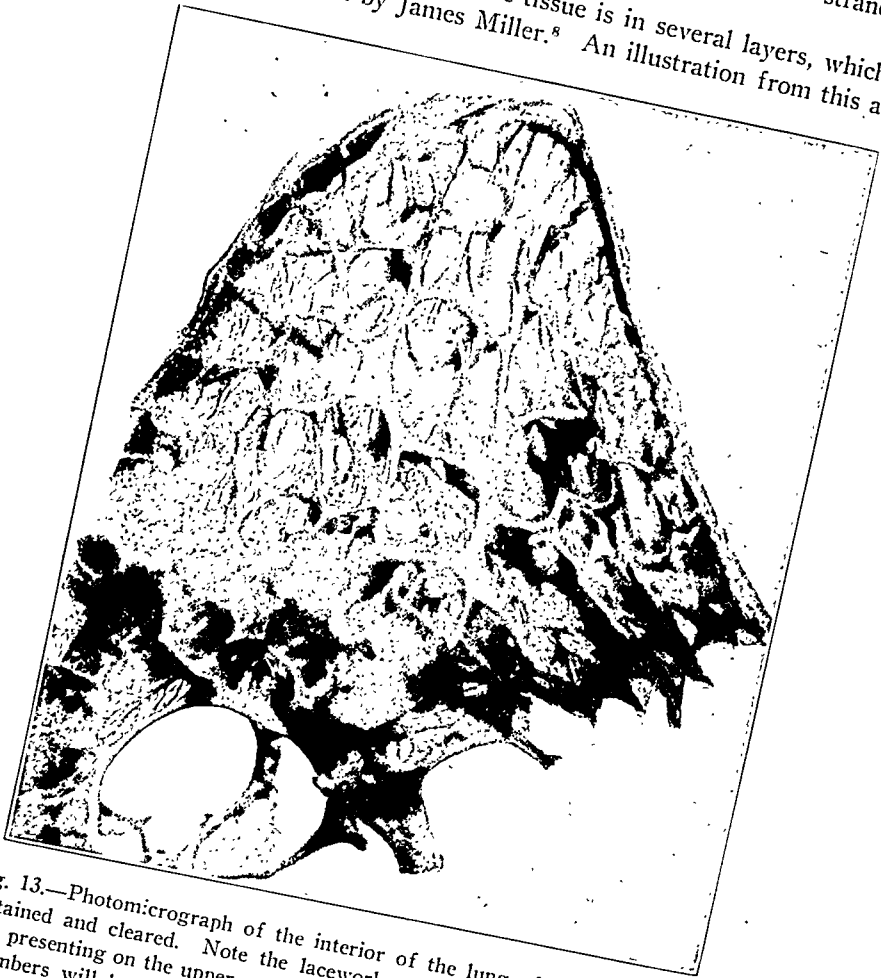


Fig. 13.—Photomicrograph of the interior of the lung of a turtle, which had been stained and cleared. Note the lacework of muscle (interwoven with elastic tissue), presenting on the upper surface. The more or less complex and subdivided air chambers will be seen through the meshes. (Author's preparation.)

is reproduced in figure 15, and shows exceedingly well these different layers in the wall of a large bronchus. The most striking and con-

⁸ Miller, J.: The Arrangement of the Elastic Fibers in the Bronchi and Lung, *J. Anat.* 40:162, 1905.



Fig. 14.—Photomicrograph of a section through the myo-elastic network lining such a loculus of turtle lung as that seen in figure 13. Note the dense muscle, and the apparent stalk, which is a partition between adjacent air chambers. Compare with figure 18, which shows the elastic tissue in a similar region.

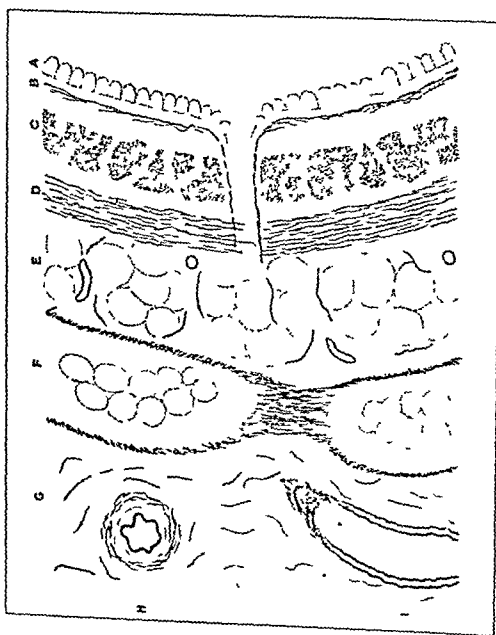


Fig. 15.—This is figure 1, from the article by James Miller in *J. Anat.* 40:164, 1906. *A* indicates epithelium; *B*, sub-basement membrane layer; *C*, longitudinal layer; *D*, muscular layer; *E*, stratum of mucous glands containing a few irregular fibers and those in connection with vessels; *F*, layer enclosing cartilage nodules; *G*, fibrous tissue of wall containing some irregularly-running fibers, also vessels; *H*, bronchial artery, and *I*, pulmonary artery. The elastic membrane *C* and the layer of elastic fibers in the muscle *D* should be noted. See text for discussion.

spicuous layer is situated in the mucosa, and is made up of strands which run longitudinally, and which are closely interfelted. The cut ends of this stout layer, which is known as the elastic membrane of the bronchial tree, are well shown in figure 15, in the layer labelled "c." It is continuous, as a distinct membrane, though diminishing in thickness, throughout the bronchial tree to the finer tubes, and in the lobule it blends with the other layers to form the network which is interwoven with the muscle already described. This layer, of course, branches with the branching of the air tubes, and always keeps the same relation to the other layers of the wall. It is plainly seen in all bronchi stained for elastic tissue. This layer can be dissected out in the fresh bronchial tree of a large animal such as the pig, and then is found



Fig. 16.—Spread preparation of elastic membrane from a large bronchus of the pig, stained with resorcin-fuchsin and teased, after having been cleared in oil of wintergreen. (Author's material.)

to possess the capacity to recoil, when stretched, in a marked degree. If stained with resorcin-fuchsin, and the fibers separated by teasing with needles in clearing fluid, as oil of wintergreen, after preliminary dehydration and treatment with benzene, a preparation is made which appears, under the microscope, as in figure 16. It will be noted both in this and in figure 15 that the ultimate elastic fibrils are fine, but of somewhat variable thickness, and that they branch characteristically; furthermore, they are grouped in fasciculi, which also branch. This provides for dilatation of the tube, in addition to lengthening.

Outside of this elastic membrane is a layer of elastic fibers which run mainly circularly (fig. 15, *d*), and which are interwoven with the muscle, as already described. In the trachea they are plainly seen in

the flaccid part of the wall. They run through and through the muscle. This layer continues on into the lobule, and blends with the elastic membrane as described. The conspicuous network which it forms in the muscle of the lobule is seen in figure 17, from a preparation of the lung of the cat similar to that shown in figure 12, but stained specifically for elastic fibers. These two figures should be compared for an understanding of the relation of the elastic fibers to those of the muscle. A cross-section of the elastic tissue and muscle in the turtle, showing the elastic tissue with ends cut across, which appear in the figure as black dots, or star-shaped structures is seen in figure 18. As already

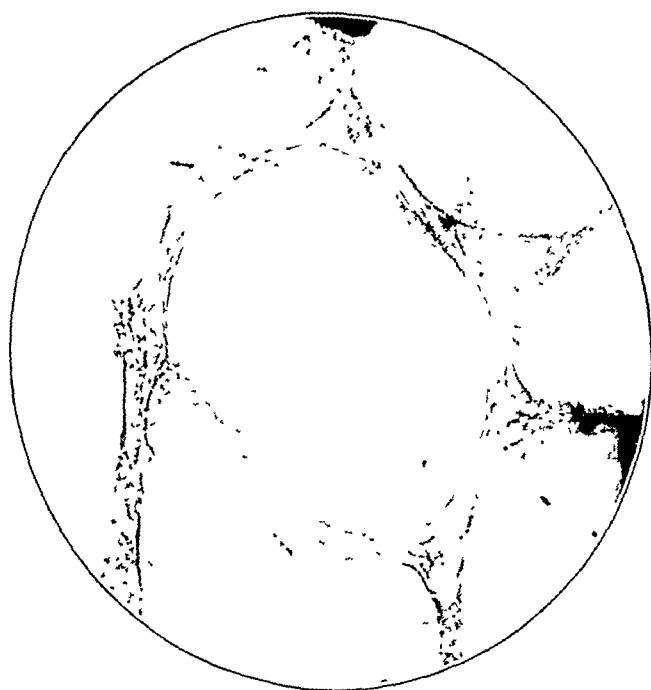


Fig. 17.—Photomicrograph of a preparation of cat's lung, showing a ring of elastic tissue leading into an air chamber. Stained with resorcin-fuchsin and cleared. Muscle does not show. Compare with figure 12, which is from a similar structure, but stained to bring out the muscle. (Author's material.)

stated, this structure in the turtle is relatively heavier than in the mammal, but the general relationship of muscle and elastic tissue is the same. The elastic tissue, here, is particularly dense in the peripheral region of the fasciculus, as shown.

Other layers of elastic tissue have been described, particularly in the larger tubes (fig. 15). Although many fibers run obliquely, the characteristic directions are longitudinal and transverse. They are obviously built to permit of changes in length and width in these tubes. Their function, in association with that of the muscle, will be considered in the next section.

Thus there is in the lung a great muscular organ, or, more accurately, a great elasticomuscular organ, the general form of which is a replica of the entire bronchial tree. If one were able to dissolve away all other tissues from the bronchial tree except this organ, the form of the tree would still be preserved accurately and completely. It is a mere platitude to say that this organ is found in all parts of the lung, for it, itself, composes an integral part of the lung tissue. Indeed, the term lung tissue means nothing more nor less than the interdigitated, complexly branched, lung lobules, or terminal branches and leaves (alveoli)

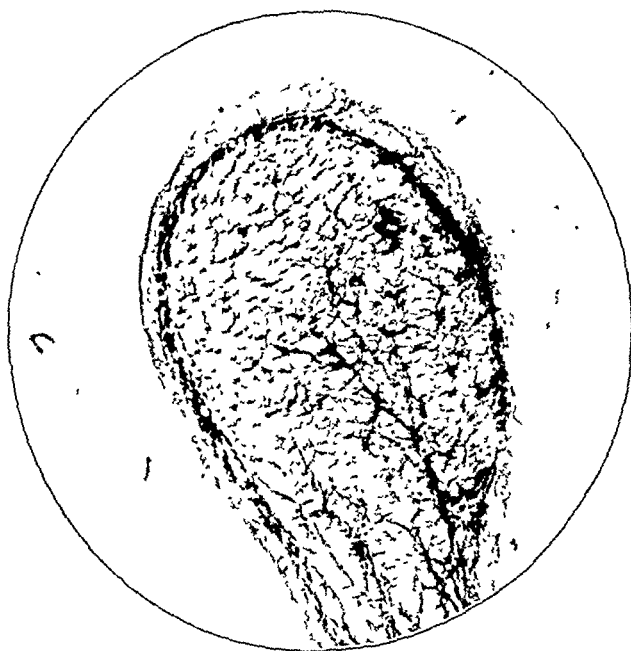


Fig 18—Somewhat oblique section through elastic net of turtle lung, stained to show elastic tissue, which appears as dark dots and stellate structures. There is a heavy band on the periphery. Compare with figure 14, which shows the muscle in a similar piece of material (Author's specimen)

of the bronchial tree. If one could disentangle these lobules, with their associated blood and lymph vessels, nerves and supporting tissues from one another, there would be no "lung substance" left, apart from them.

This organ forms an important part of the walls of the air conduits, through which air is constantly ebbing and flowing. Because it is this type of motion, there must be provision for enlargement and diminution of the lumen of these tubes, and this recoil and motor mechanism is the basis for this provision. All the space within the bronchial

tree save that within the alveoli is really the anatomic dead space, and that this is a variable space—not at all a fixed space as some believe—will be shown. All lungs are built on this fundamental plan, even down to the most simple, as that of the frog. This motor organ is found throughout all the lung-endowed group of animals; it is universal in its distribution and may well be regarded as indispensable to life.

FUNCTION OF THE BRONCHIAL MUSCLE

The function of the bronchial muscle and its associated elastic tissue is bound up with the movements which occur in the bronchial tree. Those in which muscle action may be involved are as follows: (1) changes in length; (2) changes in width, and (3) peristaltoid movements.

When one examines the roentgenographic, bronchoscopic and other evidence, it is found that there is, in inspiration, an elongation and a widening of the air tubes, and, in expiration, a shortening and narrowing of them. These movements occur, of course, only in active parts of the lung, that is, only in those parts of the lung into which air is entering, or from which air is leaving. It follows that, in ordinary quiet respiration, since some lung regions are quiescent, no movement of this kind will be found in the tubes supplying them, and, if the ebb and flow of air is slight in any region, there will be a corresponding slightness in the movement in that part: indeed, it may well be that changes in width, particularly, are at times absent. But the general principle remains that there can be no natural ventilation of any part of the lung without an elongation of the tubes supplying it. When the healthy lung is undergoing maximal ventilation, as in prolonged vigorous exercise, all the tubes, including the trachea and main bronchi, are stretched in inspiration, and are shortened in expiration. With the elongation there is widening, and with the shortening, narrowing. When one stops to think about the matter, it is apparent that the lung could not be inflated if the bronchial tubes were rigid—like gas pipes, as Reisseissen⁹ more than a hundred years ago, and as Chevalier Jackson¹⁰ recently, pointed out. Ventilation under such conditions would be limited to a thin layer of subpleural tissue. On the other hand, it is impossible to conceive of a lung, once inflated, as being deflated without a shortening of all of the tubes supplying the lung regions from which air is flowing out. With inflow of air, then, into any part of the lung, there is elongation and widening of the tubes carrying that air; and, with outflow of air from any part there is coincident

9. Reisseissen, F. D.: *Ueber den Bau der Lungen*, Berlin, 1822.

10. Jackson, C.: *The Bronchial Tree—Its Study by Insufflation*, Tr. Am. Laryngol. A., 1918, p. 319.

shortening and narrowing of the tubes. These movements are indissociable from respiration.

In inspiration there is a flow of air into the lung because the pressure in the outside atmosphere is greater than that in the lung tissue. This air pressure distends the distensible parts of the lung lobule, and the effect of the swelling of adjacent air chambers is to stretch the tubes on which they abut and to which they are attached. It also has the effect of dilating the air channels, which action, in the tubes of the lung lobule, is probably accomplished by the centrifugal pull on their walls arising from the distention of the outlying and attached air chambers.

Now, in the elongation and dilatation of inspiration it cannot be said that the muscle plays an active part; on the other hand, the most that could be expected of the muscle is that it should relax, during inspiration, in order to offer no obstruction to the inflow of air. The myo-elastic tube, as we have seen, is built to permit of being stretched, the meshes of the muscle opening out, and the longitudinal elastic tissue elongating. But in expiration it is another matter; the muscle is in a position to narrow and to shorten the tubes when it contracts. Its shortening action is slight, or perhaps almost nil, in the larger tubes; indeed, in the trachea, it can hardly exert any shortening influence except possibly slightly at the carina. But in the smaller tubes, where the strands run obliquely, contraction of the muscle must necessarily shorten them. An orderly, progressive contraction, beginning at the periphery of the air tube system and sweeping toward the trachea would diminish the volume of air in the bronchial tree, particularly in the peripheral part, or lung lobule. This movement must be sharply distinguished from a spasm of the muscle, particularly in the peripheral bronchioles, such as occurs in asthma, which has the effect of trapping air in the lobule and distending the alveoli, instead of evacuating the lung of tidal air. Such an orderly, expulsive, movement would act in conjunction with the elastic tissue. In inspiration the longitudinal fibers are put on the stretch by the lengthening of the tubes, and the circular and oblique fibers are similarly influenced by the dilatation of the tubes. In expiration, therefore, these stretched fibers recoil, and the tubes are shortened and narrowed. Indeed, most of the shortening action in the larger tubes is probably due to the recoil of the stretched elastic tissue. In the terminal chambers of the lobule, the alveolar sacs, the recoil of the elastic tissue and the contraction of the muscle have the effect of narrowing the mouths of the alveoli, changing the latter from the shape of a saucer to that of a cup. In this way the alveoli are ventilated with little or no stretching of their walls. Indeed, the mesh of the myo-elastic net is a ring, surrounding the opening into the air chamber, and this ring may be looked on as

a sphincter, although it never completely closes, but merely widens and narrows. This round-meshed fabric forms the tubular "lining" of the alveolar sacs and, even more typically, of the alveolar ducts. The dilatation and lengthening of this tubular network is accompanied by an opening up of the orifices into the air chambers, while, contrariwise, the shortening and narrowing of this net is associated with a narrowing of all of these openings.

Thus, in inspiration, the entire bronchial tree, even to its end twigs, lengthens and dilates. Its capacity is increased—in forcible breathing greatly increased. This movement has been graphically shown by different methods at this meeting by Francis, Heinbecker and Hudson, the last mentioned using motion pictures made by a most ingenious method. In this way the air has freedom of entry, and the alveoli have efficient ventilation. In expiration the tubes shorten and become narrowed; the "dead space" is diminished, and the used air driven out. The greatest amount of volume change is in the lobule—the true pulmonary bellows. The lumen of this is the most variable part of the dead space. In this process of expulsion the elastic tissue, of course, plays an important part, but it seems within the bounds of reason to assume that the bronchial musculature may also act. The muscle system would thus function as a deflation agent. If it does not do so then this elaborate motor system must be looked on as being of use only in emergencies, or as having some mysterious function that is not at all understood at the present time.

Peristaltoid Movement.—It has been known for some time that the bronchial tubes have a way of freeing themselves from harmful exudates, or injected foreign materials, other than by the act of coughing, or by the action of the cilia. This third device is a continuous wave motion, traveling from the periphery toward the center. It has been demonstrated by Reinberg,¹¹ and by Bullowa and Gottlieb,¹² in different animals by the use of x-rays after experimental procedures, and, more recently by Hudson, with motion pictures. This movement, undoubtedly, is engendered by the bronchial musculature. It has been demonstrated only in the tubes of size sufficiently large for roentgen observation, but there is no reason to suppose that it is not also found in the smaller tubes, even to the ramifications of the pulmonary lobule. It must be looked on as an important safety mechanism of the lung, and it is probable that it is of invaluable aid in ridding the air passages of exudate, as in the later stages of pneumonia. This movement is

11. Reinberg, S. A.: Roentgen-Ray Studies on Physiology and Pathology of the Tracheo-Bronchial Tree, *Brit. J. Radiol.* **30**:451, 1925.

12. Bullowa, J. G. M., and Gottlieb, C.: Roentgen-Ray Studies of Bronchial Movements, *Am. J. M. Sc.* **160**:98, 1920; Additional Experimental Studies in Bronchial Function, *Laryngoscope* **32**:284 (April) 1922.

said to be increased in gangrene and abscess of the lung, and to be diminished in bronchiectasis, where the muscle is degenerate. It undoubtedly acts in association with the cilia and with coughing. There has been demonstrated, too, by experimental procedures, a similar peristaltoid movement, going on constantly but unobtrusively, under ordinary conditions, and seeming to act in gently wafting air outward. The true meaning of this is not known. Is it the same movement as that more forcible peristaltoid action which removes exudates? It would seem closely related.

Other suggestions of uses for the bronchial musculature, particularly the more peripheral portions of this, have been made. For instance, it has been thought that, in some way, it might regulate the air tension in the alveoli. In the porpoise, Wislocki¹³ (who kindly allowed me to read his unpublished manuscript) has recently shown that the sphincteric rings in the lobule are heavy, and can, apparently, close completely, thus locking air in the terminal chambers and preventing it from being forced out by the heavy external pressure to which the lung is subjected when the animal dives deeply. But this, as Wislocki properly observed, must be looked on as a special adaptation on the part of the porpoise. It does not seem at all likely that, in the land mammals, the rings of muscle in the walls of the alveolar ducts close at the end of inspiration; rather it would seem that they remain wide open.

Another function suggested is that of control of the airflow in the bronchial tree, like that of blood in the arterial system. It might be thought, for instance, that by relaxation of the system in certain parts, and contraction in others, the air might, under the control of the broncho-motor nerves, be diverted to special areas of the lung in the same way that blood is diverted through the action of the vasomotor nerves on the arterioles. This must be regarded as a speculation, at present. Though we know that much of the lung, under conditions of quiet breathing, is at rest, there is nothing to show that the air tubes in these quiescent parts are closed off through muscle contraction. It has been suggested, too, that indirectly the bronchial musculature may influence the blood flow in a somewhat similar manner, and that it may in this way, in some measure, have the effect of a vasomotor system.

Nervous Control.—The bronchial musculature is richly supplied with nerves, both from the vagus and from the sympathetic systems, and has both dilator and constrictor fibers. The vagus has long been looked on as a bronchomotor nerve, and its ramifications extend to the uttermost reaches of this motor system. It undoubtedly carries broncho-

13. Wislocki, G. B.: On the Structure of the Lungs of the Porpoise (*Tursiops truncatus*), *Am. J. Anat.* **44**:47 (July 15) 1929.

constrictor fibers, and probably bronchodilators also. The functional character of the fibers varies in different species.

As for the afferent impulses from the muscles, there are those who regard the vagus as carrying some, at least, of these, and also those who deny such a rôle to this nerve. The sympathetic is also looked on as carrying afferent impulses. The literature on the subject of bronchial innervation is extensive, and references may be obtained in my original article. Through the action of this system of nerves the various movements of the bronchial musculature are controlled, and the volume of the dead space influenced.

That there is an elaborate system for coordinating the action of this musculature in the various movements described there can be no doubt. It is probable, too, that the functional condition of this motor organ, whether in relaxation or contraction, is made known to the central nervous system, and appropriate reflex action initiated, not only within the lung, but also in the thoracic wall and floor, i. e., in the muscles of inspiration. In this way, probably, there is brought about a coordination between the intrapulmonary and extrapulmonary respiratory motor systems. When the intercostal muscles and diaphragm contract, and air enters the lung, the bronchial musculature may be assumed to relax; and, on the other hand, when the chest wall and floor relax, and when air is leaving the lung, there may be a reflex and orderly contraction of the musculature of the bronchial tree. Here is an interesting suggestion of an antagonistic action on the part of the intrinsic muscle of the lung in cooperation with the motor mechanism of the thorax that will bear further study.

PHARMACOLOGY AND PATHOLOGY

Pharmacology.—The enormous and important literature on the action of drugs on the bronchial musculature must be passed over briefly. The drugstuffs may be divided into the constrictors and the dilators. Five types of constrictors have been recognized, depending on their site of action, i. e., (1) on the vagus endings; (2) on the muscle itself; (3) on the sympathetic, producing inhibition; (4) on the central nervous system, and (5) on some unknown site. Most of these classes have numerous members. As for the bronchodilators, there are some seven types, as follows: (1) acting on the sympathetic nerve endings; (2) inhibiting the vagus; (3) acting on the ganglion cells; (4) acting on the muscle directly; (5) showing a reversible type of action; (6) showing a double action, constriction followed by relaxation; and (7) those with an unknown site of action.

The action of epinephrine is interesting, because it has been held that, in asphyxia, it is liberated in increased amounts and it may thus,

through its bronchodilator action, be the active instrument in a safety mechanism, facilitating the air inflow in this emergency.

Pathologic Changes.—Much has been written on the changes in the musculature in pathologic states. The spasm of asthma has been referred to; it may be that this is relieved, in some cases, automatically by the physiologic outpouring of epinephrine. Hypertrophy of the bronchial muscle has been found at autopsy. In anaphylaxis, too, we have in animals showing a rich bronchial musculature a liability to anaphylactic phenomena centering in the lungs. Hypertrophy of the bronchial musculature has also been found in many other pathologic conditions, as brown induration of the lung, parasitic infections, desquamative pneumonia, etc. Atrophy has also been described, as in bronchiectasis and emphysema, though, in cases of the latter, hypertrophy has been found.

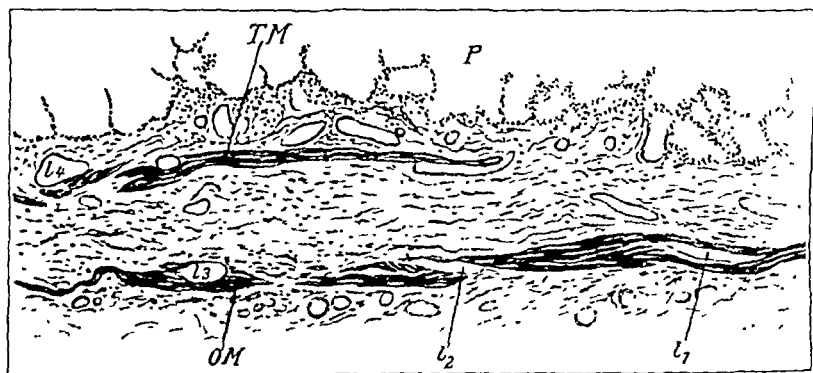


Fig. 19.—(From Baltisberger, abb. 16, p. 278.) Drawing from a section of lung of human being, showing the interstitial muscle in the visceral pleura. The dark strands are muscle. OM indicates the superficial layer of musculature; TM, deep layer; l_1 to l_5 , lymphatics of superficial plexus; l_6 , lymphatics of deep plexus; P, parenchyma of lung.

INTERSTITIAL MUSCULATURE

The system of fine wisps of muscle lying outside of the walls of the bronchial tree, known as the interstitial musculature of the lung, has been referred to. These filaments are seen in the interlobular septums, in the bronchial and vascular sheaths, and in the visceral pleura. This muscle is inconspicuous in any one point, but when considered in its entirety it forms an appreciable tissue element in the lung. A specimen from the visceral pleura is shown in figure 19. The function of these scattered fibers is not known, but may be assumed to be associated closely with that of the musculature of the bronchial tree.

CONCLUSION

This broader conception of the bronchial musculature may be of help in attacking problems centering in the lungs, as those of pneumonia, tuberculosis, or the sudden phenomenon of massive collapse, or atelectasis, which has recently been written on at great length by a number of workers, and discussed at this meeting. There seems reasonable ground for assuming that this condition may be associated with a contraction of the bronchial musculature. With the reawakening of interest in this important motor organ, we may expect much new information of a practical character regarding its functions in the healthy lung, and its derangements in the pathologic organ.

CIN-EX CAMERA STUDIES OF THE TRACHEO-BRONCHIAL TREE *

W. A. HUDSON, M.D

AND

HANS A. JARRE, M.D.

DETROIT

The Cin-ex camera is an apparatus designed to secure rapidly serial roentgenograms on film bands with the hope of obtaining physiologic records along with the anatomic records. Dr. Jarre has had the procedure in mind for several years, but, only recently, our desire to record, if possible, changes in contour and size of the tracheobronchial tree during respiration, has led to the development of the apparatus which Dr. Jarre named the "Cin-ex camera." We have endeavored to make successive records of functional changes at such short intervals as would enable us to interpret the motor phenomena themselves rather than to produce a true moving picture. The apparatus, together with some of the studies conducted up to that time, was presented to the staff of the Grace Hospital and the Detroit Roentgen-Ray Society on April 19, 1929, and will be described in detail in the roentgenologic literature. We are somewhat reluctant about promising too many advantages from the use of this method of study, but, as we hope to point out, we feel that there are certain definite advantages to be had from its use. The value depends on the manner in which the method is applied and on the proper interpretation of the results. In our studies of the tracheobronchial tree, we have undertaken to apply this method of study to one of the more difficult subjects.

Numerous observations have been recorded that would indicate the presence of a complex peristaltic action in the tracheobronchial tree. Chevalier Jackson¹ has repeatedly described a widening and narrowing of the bronchi as observed through the bronchoscope, and we are certain that all endoscopists have observed these changes. These are best illustrated by Dr. Jackson's drawings to show the effects of these motions on the relationship of a peanut in the bronchus to the walls of the bronchus during inspiration and expiration; that is, the presence of forcep spaces during inspiration and their absence during expiration.

* From the Divisions of Roentgenology and Thoracic Surgery of the Grace Hospital.

1. Jackson, Chevalier: *Bronchoscopy and Esophagoscopy*, ed. 2, Philadelphia, W. B. Saunders Company, 1927.

In 1920, Bullowa and Gottlieb² studied the tracheobronchial tree in dogs under the fluoroscope and by means of roentgenograms after the injection of the bronchial tree with an opaque medium. They described: (1) a bellows-like action of the trachea and bronchi (dogs under anesthetic) which may be limited by contraction of the bronchial muscles and (2) a peristaltic action of the bronchial muscles which seemed to be adequate to empty the bronchi without involving ciliary motions.

In 1922,³ they continued their observations by cauterizing the bronchial walls, thus severing the musculature, and they found that this interfered with the emptying of the bronchus thus treated. They regretted that they were not able to record frequently pictures with the x-rays so as to catch the changes due to motion.

Heinbecker⁴ showed by the use of injections of iodized poppy seed oil 40 per cent into the bronchi that a wider shadow is cast by the larger bronchi at the end of full inspiration than at the end of full expiration.

Reinberg⁵ described a peristaltic wave which he said resembles that seen in the intestinal tract.

William Shaw Miller,⁶ after a long painstaking study of the anatomy of the musculature of the tracheobronchial tree, found that the bronchial musculature is arranged in a network of geodesic bands which prevent any tangential motion and in this way provides for the greatest amount of extension and contraction of the bronchi.

The muscle⁷ bands form a sphincter about the openings of the alveoli into the bronchioli respiratorii and ductuli alveolares and also about the openings of the atria. He concluded that the action of the bronchial muscle in expiration is active and not passive, and he remarked that its action in the regulation of the tension of the air within the atria and air sacs deserved more attention.

Macklin⁸ studied the elastic membrane of the tracheobronchial tree and concluded in 1922 that (1) the bronchial tree stretches during inspiration and contracts during expiration, the greatest excursion being at the terminal extremities of the limbs; (2) that with a rigid tube, like a gas pipe, expansion and contraction would be impossible and (3) that

2. Bullowa, J. G., and Gottlieb, C.: Roentgen Ray Studies of Bronchial Function, *M. Rec.* **97**:251, 1920.

3. Bullowa, J. G., and Gottlieb, C.: Additional Experimental Studies in Bronchial Function, *Laryngoscope* **32**:284, 1922.

4. Heinbecker, P.: *J. Clin. Investigation* **4**:459, 1927.

5. Reinberg, S. A.: *Brit. J. Radiol.* **30**:451, 1925.

6. Miller, William Shaw: Harvey Lectures, 1924-1925; *Am. Rev. Tuberc.* **11**:1, 1925.

7. Miller, William Shaw: *Am. Rev. Tuberc.* **5**:689, 1921-1922.

8. Macklin, C. C.: *Anat. Record* **24**:119, 9122.

the main stem bronchi possibly shift forward and outward in inspiration, thus providing for expansion of the vertebral and mediastinal region of lung tissue.

Macklin did not feel, at that time, that the view of Miller,⁷ and Keith,⁹ that there occurs a widening and narrowing movement at the angles between diverging bronchi, had been clearly demonstrated. In later observations, in which he made roentgen studies, in full inspiration and full expiration on the same subject, he described the following motions: (1) elongation of the trunk and its branches during inspiration and a corresponding shortening of these structures during expiration; (2) dilatation of the bronchi during inspiration, narrowing during expiration; (3) a downward motion of the lower end of the trachea, and



Fig. 1.—Normal right lower bronchus, mapped out by iodized oil, showing two extreme phases of one respiratory cycle, *A* indicating deep inspiration and *B* complete expiration. The following should be noted: 1, difference in size and shape of the marked bronchus; 2, effect of rotation on relationship of bronchi; 3 and 4, approximation of the marked bronchi and differences in width and shape; 5, angle changes from 42 to 60 degrees and 6, separation and overlapping of the terminal bronchi during different phases of respiration.

main bronchi and lung root, in passing from expiration to inspiration, and an upward movement in passing from inspiration to expiration and (4) the interbronchial spaces show widening in inspiration without material alteration of direction of the bronchi.

In January, 1929, Macklin¹⁰ gave a most extensive review of the literature on the musculature of the bronchi and lungs.

9. Keith, A.: *The Mechanism of Respiration in Man*; in *Further Advances in Physiology*, G. L. Hill, 1909.

10. Macklin, C. C.: *Physiol. Rev.* 9:1 (Jan.) 1929.

In 1925, McClintock,¹¹ in a study of the anatomy of lobar pneumonia, concluded that the lung possesses a peristaltic mechanism.

Thus it will be noted that there have been ample observations to indicate the presence of motion in the tracheobronchial tree. There has been some variance in opinion as to the exact nature of this motion, and it remains for us to record the different phases of the motions before we can properly interpret them and set aside these variances.

We must warn physicians not to expect such striking motor phenomena in the tracheobronchial tree as can be observed in the stomach

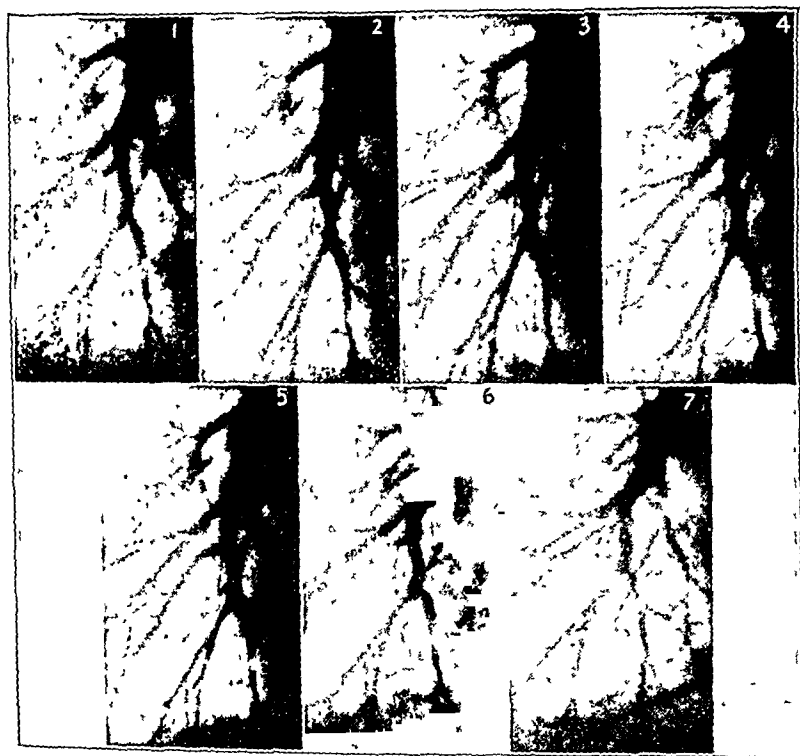


Fig. 2.—Demonstration of the functional behavior of a normal right lower bronchus (filled with iodized oil) during one respiratory cycle. (Section from a film-band 8 inches by 20 feet obtained with the Cin-ex camera.)

or intestines, as we are dealing with a smaller body of muscles and a smaller lumen in the object being studied.

It is obvious that the influence of this mechanism, when applied to a gaseous body, will be manifest in a manner different from that when it is applied to a liquid or viscid body. Again one might assume that the chief influence of any form of immobilization of the lung will be exerted

11. McClintock: Anatomy of Lobar Pneumonia, Michigan State M. J., 1925, p 643.

on the passive elements of motion, while the active elements of bronchial motion will remain, and might in time compensate in part for the lost passive motion.

In our studies we first used a normal dog weighing about 10 Kg. We made a series of exposures at the rate of one per second, following which 10 cc. of iodized oil was allowed to flow into the tracheobronchial tree and the records continued. A difficulty encountered in this work was the rapid respiration in the dog. This led us to make studies on the human subject, who can regulate his rate of respiration. We have found this to be an advantage in that the slower rate of respiration permits more exposures during a single respiratory cycle.

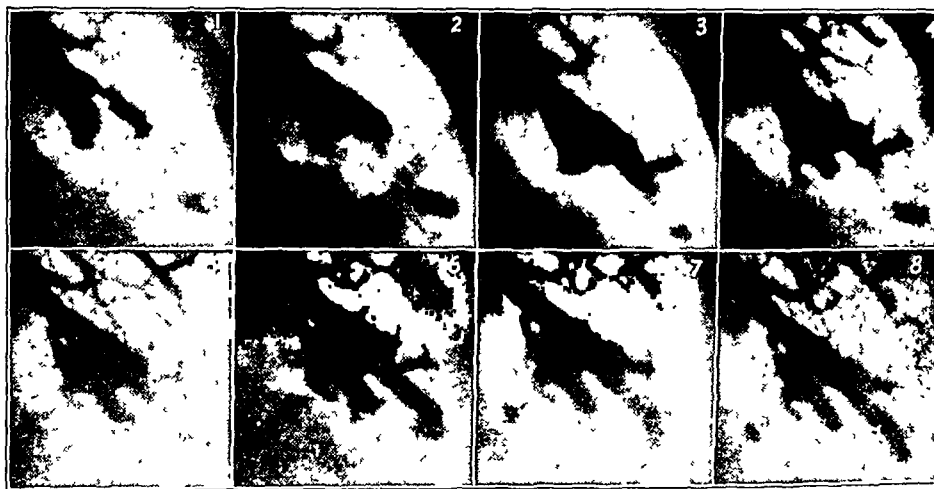


Fig. 3.—Demonstration of the functional behavior of an ectatic bronchus during respiration and gradual influx of iodized oil. (Sections from a film-band 8 inches by 20 feet obtained with the Cin-ex camera).

Serial x-ray pictures of the chest of a dog, made at the rate of one each second and with an exposure of one tenth of a second, revealed no abnormal markings, and it was particularly noted that the movement of the wall of the chest and the contents of the thorax during respiration caused no blurring of the pictures that interfered with the interpretation of the shadows present. The first series of x-ray pictures consisted of twenty-four exposures completed within twenty-four seconds from the time of the first exposure.

We next passed a small rubber catheter through the dog's laryngeal aperture into the trachea and made a second series, while 10 cc. of iodized oil was allowed to flow into the right stem bronchus. We have seen in this series of x-ray pictures that there occur regularly, along the

secondary bronchi, points of narrowing, this phenomenon being present chiefly during expiration; during inspiration, the walls become parallel to each other or nearly so. This phenomenon, as we have seen it in the dog, is not so clearly defined as we would like it to be. As the number of exposures which we were able to make during a respiratory cycle was limited by the frequency of the dog's respiration, we next turned our attention to the human being. We hoped that by so doing we might be able to secure more exposures during a respiratory cycle and to obtain more clearly defined evidence of motion inherent in the bronchi.

The first subject was a woman about 22 years of age. She was in good health and entirely free from any symptoms of pulmonary infection.

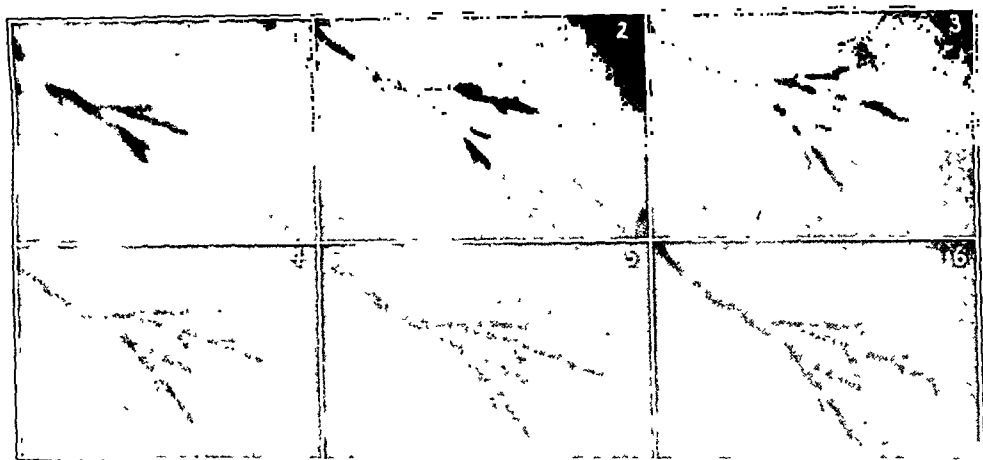


Fig. 4.—Demonstration of the functional behavior of an asthmatic-spastic-bronchus during respiration and gradual influx of iodized oil. (Sections from a film-band 8 inches by 20 feet obtained with the Cin-ex camera.)

Roentgenograms made immediately before the injection of iodized oil revealed no abnormal markings within the pulmonary field. Serial studies made while iodized oil was allowed to flow into the right stem bronchus through a catheter revealed a number of interesting facts:

1. There were noted regularly occurring narrowing, of all bronchus which seemed to originate in the peripheral portions of the bronchial tree and to be associated with the propulsion of the oil toward the trachea. We also observed that this phenomenon was not of equal intensity in all parts of the bronchial tree at any one time. The regularity with which these narrowings occurred was such that one could determine the phase of respiration during which any given roentgenogram was made by their appearance. During inspiration the walls of the bronchi were

for the most part parallel and showed but few irregularities, while during expiration the walls lost their parallel relationship and just at the end of expiration seemed to come so closely together in some areas that they almost touched each other. We interpreted this phenomenon as evidence of a peristaltic-like action of the musculature of the tracheobronchial tree. From its influence on the oil in the tracheobronchial tree it would seem that it was sufficient in itself to empty the bronchial tree of secretions under ordinary circumstances without invoking other aid.

2. We also saw in these studies an alteration of the angles of diverging bronchi of the lower lobes. During inspiration the angles became smaller, that is, of an acute nature, while during expiration they became greater. We noted changes in one angle from 41 to 81 degrees. The question immediately arises as to whether or not a rotation of the bronchial tree might not account for these changes in the angle. It is evident that rotation would cause apparent, but not true, alteration, in the size of the angles of diverging bronchi. At the same time, however, were the changes due to rotation, we would expect to see some angles become smaller while in another part of the field we would see the opposite. In these studies there was noted a uniform alteration of the angles in all parts of the field being studied. For this reason we feel that rotation is not sufficient to account for the changes noted.

3. Definite evidence of rotation of the tracheobronchial tree was seen. This was best brought out, in the lower lobes, by the appearance and disappearance of certain bronchi from the line of vision during the respiratory cycle. Rotation was seen to be from the back to the front during inspiration with a definite element of descent associated with the movement, so that the movement struck a curve simulating closely a corkscrew turn.

4. The tracheobronchial tree was seen to shift in a proximal distal direction during inspiration and in the opposite direction during expiration. The shift was over a distance of at least one-half inch, as determined by measurements taken from the last cervical spine to a point in the upper portion of the bronchial tree of the lower lobe, the shift being at least three times greater for those points in the most peripheral portions of the same lobe. We must bear in mind that this shifting of the bronchial tree is intimately associated with the rotation movement of the lung and that it, together with the rotation, undoubtedly plays a big part in providing space for expansion of the lung.

5. In addition, the bronchi, particularly those lying obliquely or parallel to the diaphragm, were seen to approach each other closely during expiration and to become widely separated during inspiration. The opposite was true of those bronchi which were perpendicular to the

diaphragm. In each case the movements closely simulated the opening and closing of a fan.

6. The position of the diaphragm and the position and relationship of the ribs during the different phases of respiration were recorded.

7. The influence of cough on the degree of bronchial spasm was seen, and it was particularly noted that a suppressed cough can force material into the alveoli, though in a normal person most of it enters the trachea.

It is evident that the foregoing demonstration of a motor phenomenon in the tracheobronchial tree will be of more value if we are able to show a practical application of the information obtained. There are certain conditions under which one might expect to find interference with this motor phenomenon. For instance, in those cases of pulmonary suppuration of long standing, particularly those spoken of as chronic bronchiectasis, we might expect to find that the action of the bronchial musculature has been, to say the least, inhibited. We accordingly made a study of such a case. A girl, aged 17, had a cough productive of large amounts of thick yellow sputum over a period of from ten to fourteen years. Bronchoscopic examinations showed the pus to be coming chiefly from the posterior portions of the left lower lobe. Serial studies revealed: a large gas pipe-like bronchus leading to the posterior lateral portion of the lower lobe in which no evidence of bronchial spasm was seen. In fact, with respiration, iodized oil seemed to accumulate in this area rather than to be forced out as in the normal lung. In the lung field, adjacent to this bronchus, some irregularities in the bronchial walls were noted that might be interpreted as bronchial contractions, but these were definitely inhibited. From these observations one might conclude that the grossly involved portion of the bronchial tree would require eradication before the patient could be freed of her symptoms, whereas those portions of the lung which show some evidence of remaining, physiologic motility might be treated more conservatively.

We also made studies on a man, weighing 170 pounds, who had been told by his clinician that he had asthma. We passed a bronchoscope on this patient and repeatedly encountered sufficient bronchial narrowing of a spastic character to make it difficult to enter the stem bronchi. At the same time we clearly demonstrated that the lumen of the bronchi was of sufficient caliber to take a 7 mm. and even a 9 mm. bronchoscope. Serial studies were made in the same manner as in the normal subject and we observed: A marked degree of bronchial spasm which prevented the oil from entering any of the terminal bronchioles. The spasm was seen to involve the entire bronchial tree so far as the oil had been permitted to enter and in addition to the general spasm of the bronchial tree we saw segmentation of the bronchi so that the secondary bronchi had an appearance similar to a string of sausages. It is apparent that with such a

degree of narrowing of the bronchial tree the patient will receive relief from his symptoms when the bronchial obstruction is relieved. It is not within our province today to discuss the manner in which relief is to be obtained.

In the animated films one observes the same changes in position, size and shape of the bronchi as brought out in the study of the film slides. As we said in the beginning, we did not begin the work with the idea of producing a true moving picture. However, the animated film does make the element of motion more strikingly evident to one spending but a few moments on the subject.

While we have been able to demonstrate definitely certain types of motion in the tracheobronchial tree, we feel that this is only the beginning of the study of this subject. We do not feel justified in forming conclusions at this time; but we have felt that we are justified in presenting these studies in order to make the method known. We shall without doubt find it necessary to add to and take from our impressions as we make further observations.

ABSTRACT OF DISCUSSION

ON PAPER BY DR. MACKLIN AND THAT BY DRS. HUDSON AND JARRE

DR. E. A. GRAHAM, St. Louis: As usual, after such a demonstration as this, I should like to add my praise. I think the society owes Dr. Hudson and his associate a vote of thanks for these pictures; also to Dr. Macklin for coming here and giving us the benefit of his extensive research, which has continued over a long period of years.

Dr. Cutler and I were both curious, Dr. Hudson, to know whether or not in taking any pictures of this last patient (I mean the patient with the spasm) you used any epinephrine or ephedrine and then took some more pictures; or have you done that on any asthmatic patients?

DR. HUDSON: That is one of our future problems, Dr. Graham.

DR. C. C. MACKLIN, London, Canada: I wish to thank the association for the invitation to address you here, and I also wish to congratulate Dr. Hudson for his series of pictures. His views are illuminating to me, and I am sure they have brought to your minds a new conception of the changes which go on in the bronchial tree in the process of lung inflation and lung deflation.

There is one point I should like to bring up, and that is the necessity of dissociating accurately the behavior of the bronchial tree, on account of the presence in it of what one might call foreign substance, from its behavior due to normal respiratory action.

The work of such men as Bullowa and Gottlieb emphasizes the occurrence of peristaltoid action in the bronchial tree. I am just wondering how much of the change seen in these shadows is due to the effort of the bronchus to relieve itself of this oil.

DR. WILLIAM HUDSON, Detroit: I have little to add, except that I should like to answer Dr. Macklin's question.

As I said in conclusion, there are a good many problems that will be coming up and that are already before us at this time. Dr. Graham has mentioned one of the problems. We hope to undertake immediately the study of the use of epinephrine and other drugs to see what their action is on this spastic bronchus.

The other is this condition in the extremely dilated bronchus, for instance. What would be the effect of a phrenicectomy on that patient, and the action of that bronchus? What would be the effect of draining that bronchus and allowing continued drainage over a long period of time so that the infection has disappeared, and then repeating the study to see if there is any return of the embolus of muscular contraction? We should see if the marshy area above there would return to a normal condition.

In reference to Dr. Macklin's question about the foreign substance, it was necessary to introduce some substance that could be visualized. It is not exactly an ideal situation, but it is the one which is most available and, as I pointed out in the beginning, it is evident that the influence of the mechanism as we have pictured it when applied to a gaseous body or to a liquid body or to a viscid body would be different in any one of those conditions. If we used an irritating gas, it is obvious that the mechanism, if present, would be called into more apparent workings.

Dr. Jarre has devoted a large amount of time to the development of the mechanism whereby we have been able to record these pictures. We have brought some of the original exposures on the film bands, which were made especially for us, and we should be glad to have you see them after the meeting is over.

THE PRODUCTION OF INTRAPULMONARY SUPPURATION BY SECONDARY INFECTION OF A STERILE EMBOLIC AREA

AN EXPERIMENTAL STUDY *

EMILE HOLMAN, M.D.

AND

MARY E. MATHES, M.D.

SAN FRANCISCO

In a previously described series of experiments,¹ it was found that the introduction into the venous circulation of an embolus infected with pyogenic organisms may be followed by widely differing pathologic changes in the parenchyma of the lung (fig. 1). Around the invading embolus there may occur a local consolidation and transient pneumonitis with complete and early recovery and with no permanent pulmonary damage. Hemorrhagic infarction may occur followed either by a cicatrizing resolution or by the formation of an abscess in the infarcted area. Occasionally, there develops a massive hemorrhagic consolidation of the lobe in which the infected embolus lodges, invariably followed by death.

In attempting to explain the varying results produced by identically infected emboli, differing degrees of thrombosis within the pulmonary vessels were postulated. If thrombosis should proceed only distally from the embolus, simple infarction might be expected, whereas thrombosis both proximal and distal to the embolus might lead to an extensive hemorrhagic consolidation of the entire lobe.

To amplify our observations and to confirm or to disprove the foregoing assumptions, experiments were undertaken to determine the exact conditions present within the pulmonary vessels following the simultaneous introduction of infected and sterile emboli into the same animal.

The unexpected development of an infarction and an abscess in sterile embolic areas, due to a bacteremia from the infected embolus, led to other experiments involving two sterile jugular emboli followed or preceded by the introduction of bacterial emulsions into the femoral vein. Again abscesses occurred in the sterile embolic areas.

* From the Laboratory for Surgical Research, Stanford University Medical School.

1. Holman, E.; Chandler, L. R., and Cooley, C. L.: *Experimental Studies in Pulmonary Suppuration*, Surg. Gynec. Obst. **44**:328 (March) 1927.

METHOD

The experiments were performed on dogs under ether anesthesia. The embolus was prepared as originally described for the production of pulmonary abscesses.² The jugular vein was isolated, two segments excised and identically prepared, except that one contained one lead shot and was infected with *Staphylococcus aureus*, *Streptococcus nonhemolyticus* and *Bacillus coli*, whereas the other segment of vein contained one and one-half pieces of lead shot and was sterile. The three aforementioned strains of organisms were maintained at approximately unvarying virulence by subcultures, and the same strains were used throughout. The sterile embolus was introduced into the proximal end of the divided jugular

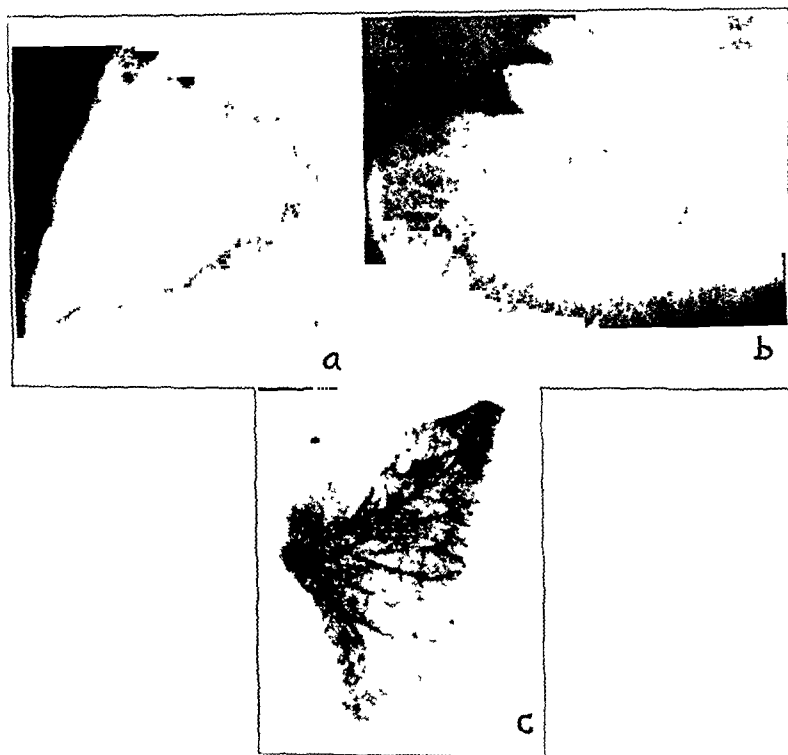


Fig. 1.—Roentgenograms of excised specimens to show the varied effects of infected jugular emboli: *a*, complete hemorrhagic consolidation with death after four days; *b*, infarction and abscess formation after nine days; *c*, complete restoration of lung to normal after sixty-three days.

vein first, and the animal was kept on one side for about ten minutes, during which time the thorax was occasionally shaken to insure the onward progress of the embolus through the heart and thence into the lungs. The animal was then turned to the other side and the infected embolus introduced. It was usually possible by this procedure to control the ultimate lodgment of the embolus in

2. Holman, E.; Weidlein, I. F., and Schlueter, S. A.: A Method for the Experimental Production of Lung Abscess, *Proc. Soc. Exper. Biol. & Med.* **23**: 266, 1926.

opposite pulmonary fields, and the subsequent identification of the emboli was made possible by the differences in the shot.

The animals were killed at varying periods and the condition of the pulmonary circulation investigated by injecting Hill's mass,³ which is a suspension of 17 per cent bismuth oxychloride in a 10 per cent solution of gum acacia. This mass fills the arterial tree down to, but not including, the capillary bed. The thorax was opened exactly in the midline of the sternum, and the descending aorta beyond the third intercostal was ligated, as were also the right innominate, the left subclavian, the left carotid and both vertebral arteries. These ligations permitted the complete injection, at a pressure of 160 mm. of mercury, of the bronchial arteries through a cannula introduced into the ascending aorta. The lungs and heart were removed en masse, the lungs were inflated and kept inflated by an intrabronchial pressure of 10 mm. of mercury. Roentgenograms of the injected bronchial arteries were made. Then Hill's mass was injected into the pulmonary artery, at a pressure of 60 mm. of mercury, the lung being kept inflated during and after the injection. Again roentgenograms were made.

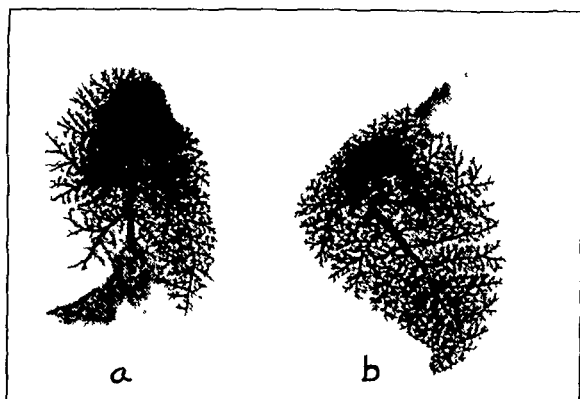


Fig. 2 (Animal K 6).—Roentgenograms of the isolated lobes twenty-four hours after the introduction of jugular emboli: *a*, infected embolus with pneumonitis surrounding it completely occluding the pulmonary artery; *b*, sterile embolus with no reaction about it but complete occlusion of the pulmonary artery.

PROTOCOLS

The following protocols illustrate our results:

ANIMAL K 6.—On Sept. 5, 1928, two emboli, the first one sterile and the second one infected, were introduced into the jugular vein. Twenty-four hours later, the animal was killed with chloroform. At necropsy, the pleural cavity was clear, without adhesions. The upper lobe contained a segment involving almost a third of the lobe, which was firm, edematous and red with extravasated blood, evidently an infarction produced by the infected embolus. There was no evidence on the surface of the sterile embolus, the remainder of the lung appearing normal. The injected specimen (fig. 2) showed that the sterile embolus had lodged in the right upper lobe occluding a second degree branch of the pulmonary artery. A similar

3. Hill, Eben: A Radiopaque Bismuth Suspension for Anatomical and Pathological Research, *Bull. Johns Hopkins Hosp.* 44:248 (April) 1929.

occlusion had been produced in the left upper lobe by the infected embolus, the artery being occluded for about 1 cm. proximal to the embolus by a retrograde thrombosis. On cut section, the lobe containing the sterile embolus showed no reaction about the shot, whereas the lobe with the infected embolus showed a mottled, yellowish-brown and red area extending out to the periphery from about the center of the lung. There was no abscess, but a marked pneumonitis and a hemorrhagic infiltration of the parenchyma surrounded the shot for several centimeters.

ANIMAL K 19.—On November 7, two emboli were introduced into the jugular vein, the one sterile and the other infected. Within eighteen hours the temperature had risen from 35.5 to 41.5 C., the pulse rate from 144 to 180 and respirations from 28 to 64. The dog died twenty-four hours after the introduction of the emboli. At necropsy, the left pleural cavity contained considerable purulent bloody fluid. The left lower lobe, which contained the infected embolus, showed an extensive hemorrhagic consolidation, although part of the lobe was still air-containing. The right upper lobe contained the sterile embolus, but there was no evidence of its presence until the pulmonary artery was injected, when it was sharply outlined by its lack of injection.

A blood culture made after the death of the animal showed a growth of all three organisms contained in the infected embolus, namely, *Staphylococcus aureus*, *Streptococcus nonhemolyticus* and *Bacillus coli*.

The injection of the bronchial artery showed no dilatation, and the pulmonary artery showed good injection up to within 1 cm. of the infected embolus. There was no injection of the pulmonary artery beyond either the sterile or the infected embolus.

There was a hemorrhagic consolidation of a portion of the left upper lobe contiguous to the consolidated lower lobe. This pneumonic area in the left upper lobe showed good injection of the pulmonary artery.

Two other animals, K 7 and K 21, both of which died forty-eight hours after the introduction of the emboli, showed a hemorrhagic consolidation of the lobe containing the infected embolus, and the pulmonary artery in each instance showed good injection up to within 1 cm. of the embolus. Moreover, in all three instances, a massive consolidation occurred in other lobes besides those containing the emboli and a good injection of the pulmonary artery in these lobes was obtained.

ANIMAL K 22.—On Nov. 19, 1928, a sterile and an infected embolus were introduced as already described. Twenty-four hours later the temperature had risen from 35.6 to 39 C., the pulse rate from 112 to 136 and respirations from 20 to 32. The dog was killed with chloroform four days after the introduction of the emboli. At necropsy, the left lower lobe contained a pyramidal-shaped area of liver-like consistency, which showed on the surface as a bright red, slightly depressed area. There was no evidence of the sterile embolus on either palpation or inspection.

A roentgenogram made after the injection of the bronchial artery showed both emboli in the left lower lobe with a marked consolidation and beginning abscess formation around the infected embolus and no change about the sterile embolus (fig. 3). There was beginning dilatation of the artery leading to the infected embolus, but dilatation was absent in the branch leading to the sterile embolus. The roentgenogram made after the injection of the pulmonary artery showed almost complete filling of the bronchial and alveolar spaces in this lobe due to a communication between a bronchus and the pulmonary artery at the site of the

abscess. A cut section through the lobe showed a small abscess lying at the apex of a wedge-shaped triangular area of hemorrhagic infarction. There was no reaction about the sterile embolus.

ANIMAL K 20.—The usual two emboli were introduced, and the animal killed eight days later. At necropsy, the left lower lobe, in which lay the infected embolus, contained a firm section 2 cm. in diameter, presenting on the surface as a red, slightly depressed area. The right lower lobe contained the sterile embolus, as disclosed on the surface by a pyramidal-shaped area slightly paler than the rest of the lung

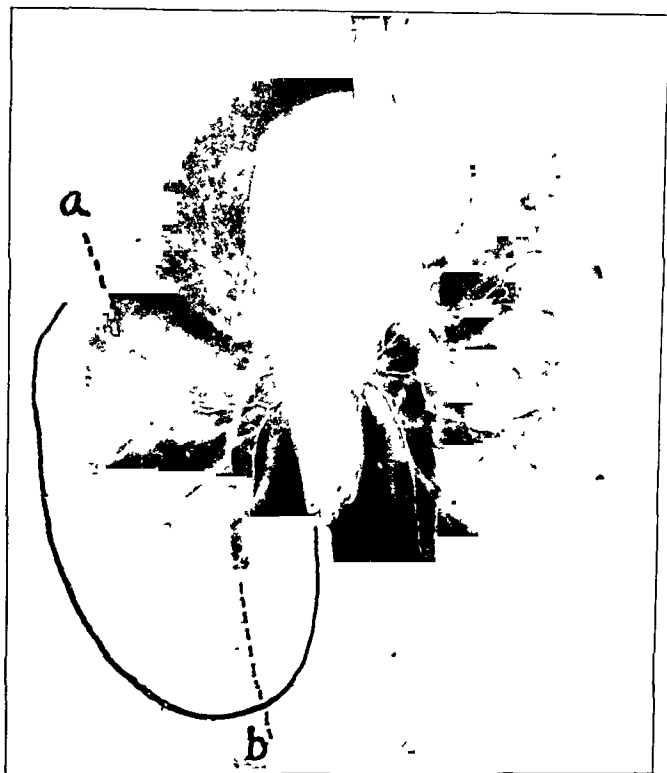


Fig. 3 (Animal K 22).—Roentgenogram of the entire lung following injection of the bronchial artery four days after the introduction of jugular emboli: *a*, marked pneumonitis with small abscess formation about the infected embolus; *b*, no reaction about the sterile embolus. Note the normal size of the bronchial artery leading to the sterile embolus, and the beginning dilatation to the infected embolus.

The roentgenogram taken after injection of the bronchial artery showed a remarkable dilatation of the bronchial artery leading to the lobe containing the abscess (fig. 4). In the region of the abscess there was demonstrated a definite anastomosis between the bronchial artery and the pulmonary artery, as shown by a localized injection of the latter through the former. A definite dilatation, though not so marked, also characterized the bronchial artery leading to the sterile

embolus. Aside from the slight injection through the bronchial artery as previously noted, the pulmonary artery beyond either embolus was not injected.

The cut section showed a large abscess, 2 by 1.5 cm., produced by the infected embolus, whereas the sterile embolus was embedded in intact pulmonary tissue which showed a slight edema and slight hemorrhagic infiltration in a pyramidal-shaped area beyond the embolus.

ANIMAL K 17.—On October 9, this animal received two emboli, according to the usual procedure. Four days later, the temperature had risen from 37.2 to 40.3 C., the pulse rate from 88 to 168 and respirations from 16 to 76. The animal was killed eight days after the introduction of the emboli. At necropsy, the pericardium was red and covered with a fibrinous exudate. The parietal pleura was also covered by a fibrinous exudate. There was a small amount of free turbid fluid in the left pleural cavity. The left upper lobe, which contained the infected



Fig. 4 (animal K 20).—Roentgenograms of the entire lung removed eight days after the introduction of jugular emboli: I, following injection of the bronchial artery; II, following injection of the pulmonary artery. Note the greater dilatation of the bronchial artery to the lobes containing the infected embolus (a), as compared with the artery leading to the sterile embolus (b). There is a slight injection of the pulmonary artery through the bronchial artery, in the region of the abscess.

embolus, was closely adherent to the mediastinum and showed an extensive gangrenous area with considerable destruction of pulmonary tissue. A small part of the lower portion of the lobe was still air-containing.

The right middle lobe, which contained the sterile embolus, showed a typical hemorrhagic infarction, comparable to the infarction produced by an infected embolus. The infarcted area was firm, deep red and nonair-containing. The bronchial artery leading to the gangrenous area was again markedly dilated, with slight but definite dilatation of the artery to the infarcted area due to the sterile embolus (fig. 5). The pulmonary artery was injected up to the location of the

emboli, but not beyond them. The cut section showed marked destruction of pulmonary tissue beyond the infected embolus, and a typical hemorrhagic infarction beyond the sterile embolus.

Before death, a blood culture in this animal was positive for all three organisms originally introduced in the infected embolus. It may be inferred, therefore,

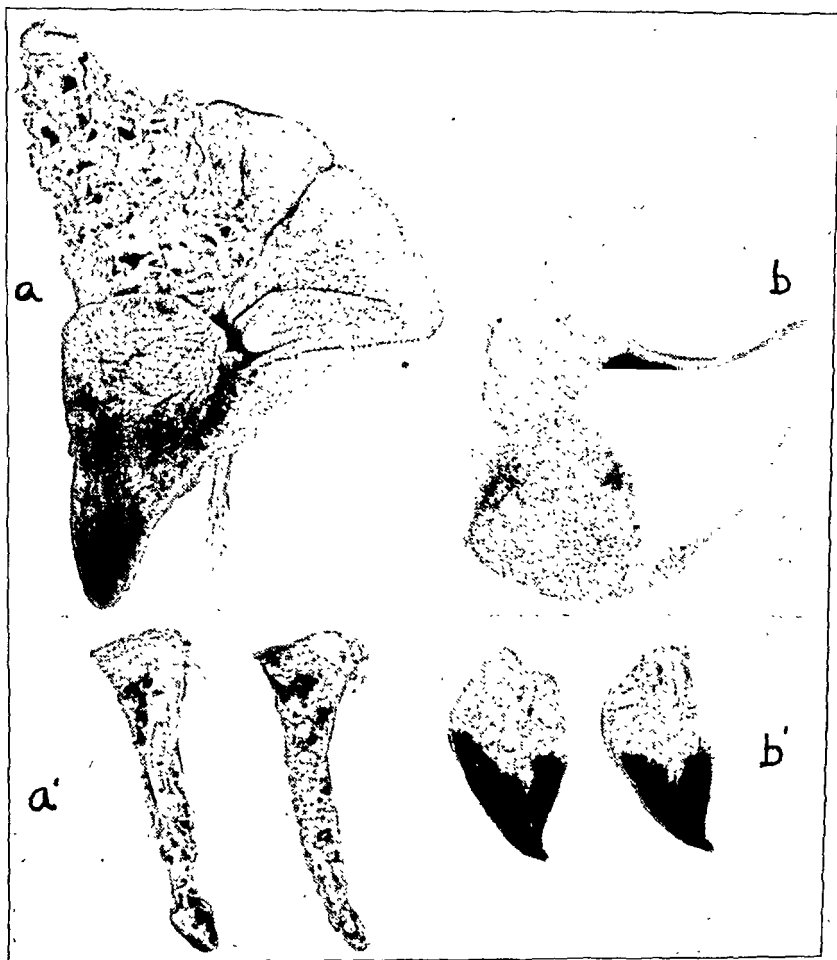


Fig. 5 (animal K 17).—Isolated lobes removed eight days after the introduction of jugular emboli: *a*, gangrene and multiple abscess formation distal to the infected embolus; *b*, hemorrhagic infarction distal to the sterile embolus; *a'* and *b'* show the cut sections.

that the hemorrhagic infarction caused by the sterile embolus was due to secondary invasion of the embolic area by circulating organisms.

ANIMAL K 18.—Two emboli, one infected and one sterile, were introduced in the usual manner on November 7, and the animal killed fifteen days later. At necropsy there were no adhesions or fluid in the pleural cavity. In the left lower

lobe, which contained the infected embolus, there was a scarred area about 4 by 2 cm. in size, firm, deep red and somewhat depressed after inflation of the lung. Before inflation, the site of the sterile embolus could not be detected, but after inflation the right upper lobe showed a pyramidal-shaped area, slightly paler than the rest of the lobe. Injection of the bronchial artery showed moderate dilatation of both branches leading to the lobes containing the emboli, and less marked in the lobe containing the sterile embolus.

There was a slightly increased density about the infected embolus, but the pulmonary field around the sterile embolus was normal. The pulmonary artery showed filling up to both emboli, but not beyond them. The cut section of the lobe containing the infected embolus showed no abscess cavity, but the pulmonary tissue beyond the embolus was slightly discolored by blood pigments and was definitely more fibrous than the normal lung. The embolic area beyond the sterile embolus was normal.

Comparable observations with almost complete return to normal of the lung beyond the infected and sterile emboli were made in three other animals: K 11 (twenty-four day specimen), K 12 (twenty-seven day specimen) and K 35 (ninety day specimen).

ANIMAL K 26.—Two emboli, one infected and one sterile, were introduced into the jugular vein on December 3. Four days later the animal was very ill with a fever of 40.4 C., a pulse rate of 136 and respirations 56. The animal remained quite ill until it was killed fifteen days after the introduction of the emboli.

At necropsy, there was a small amount of slightly cloudy blood-stained fluid in each pleural cavity. The pericardium was thickened, red and furry on its pleural surface. In the left lower lobe, which contained the infected embolus, there was a well defined, firm, dark red segment, with ulceration of the visceral pleura due to destruction of underlying pulmonary tissue. The cut section showed multiple abscesses in this area (fig. 6).

Similarly, in the right lower lobe, which contained the sterile embolus, there was a firm, dark red section, also ulcerated on its surface with several small fluctuating abscesses presenting on the surface. On cut section, one large abscess and several smaller abscesses were present. The bronchial artery was greatly dilated in the branches leading to the lobes containing the emboli, the pulmonary artery being uninjected beyond the emboli. There was apparently a thrombus in the pulmonary artery 2 cm. proximal to the infected embolus.

Again the development of abscesses in the embolic area beyond the sterile embolus can be explained only on the basis of secondary invasion of this area by circulating organisms liberated by the infected embolus. A blood culture two days after the introduction of the emboli was sterile. Unfortunately no other cultures were made, but from previous experiences¹ one may infer the presence of a bacteremia due to the abscess produced by the infected embolus.

ANIMAL K 25.—On Dec. 3, 1928, two emboli, one infected and the other sterile, were introduced into the jugular vein. Three days later the animal was quite ill, the temperature having risen to 40.6 C., the pulse rate to 160 and respirations to 56. A blood culture was positive for nonhemolytic streptococcus. Thereafter there occurred a gradual improvement, but with the loss of considerable weight and a persistent cough. After thirty-one days, the animal appeared normal and was killed. At necropsy, the left lower lobe was firmly adherent to the diaphragm and to the wall of the chest. Within the lobe at the site of these adhesions was a large, rounded, firm area, 4 cm. in diameter, which proved to be the location of the infected embolus (fig. 7). After inflation, the left lower lobe showed marked retraction and diminution in volume. The location of the sterile embolic

area was disclosed by a slightly paler color to the surface of the tip of the right upper lobe. The left upper lobe, contiguous to the lower lobe, showed a red retracted area, undoubtedly the site also of a localized pneumonitis. This involvement of a lobe adjacent to an infected area in another lobe has been frequently noted and its explanation is still wanting.

The bronchial artery leading to the lobe that contained the embolus was enormously dilated, forming a thick network of vessels around the bronchus and completely surrounding the abscess cavity which had a diameter of about 2.5 by 3 cm. The pulmonary artery showed no filling beyond either embolus.



Fig. 6 (animal K 26).—Cross-sections of lobes removed fifteen days after the introduction of jugular emboli: *a*, mottled infarction and multiple abscesses distal to the sterile embolus; *b*, multiple abscesses distal to the infected embolus.

The cut section showed a large multilocular abscess with little inflammation in the lung surrounding it, and with no communication to a bronchus. The lung around and beyond the sterile embolus was normal.

ANIMAL K 35.—This animal was killed ninety days after the introduction of a sterile and an infected embolus. The necropsy revealed an almost normal appearing lung in the deflated state, but after inflation the two embolic areas were revealed as being slightly paler than the lung proximal to the emboli.

The bronchial artery leading to the lobe containing the sterile embolus was dilated from four to five times its normal size. The pulmonary artery distal to

this same sterile embolus showed practically no filling. On the other hand, the bronchial artery leading to the lobe containing the infected embolus was about normal in size, and the pulmonary artery distal to the embolus was almost completely filled by the development of an extensive collateral circulation through anastomosing pulmonary vessels. The main pulmonary artery leading to the embolic area was still completely occluded by the embolus.

A cut section through the sterile embolic area showed the embolus surrounded by a fibrous thin wall and normal pulmonary tissue. A section through the infected embolic area showed no abscess, but a slight fibrosis of pulmonary tissue beyond the embolus.



Fig. 7 (animal K 25).—Inflated lung showing marked shrinkage and retraction of the lobe *a* containing the abscess produced by the infected embolus. The sterile embolic area at *b* was not detected in the deflated state, and presented only as a slightly paler area in the inflated state.

Comment.—A review of the experiments undertaken thus far shows the following results:

In eight normal animals that received simultaneously two sterile emboli into the jugular vein without any infecting organism, there occurred not a single instance of hemorrhagic infarction. Occasionally, on the surface of the embolic area, one observed a slightly paler color

than normal, and on cut section one noted a slight edema with an altered pigmentation, indicative of a hemorrhage into the pulmonary tissue.

A striking fact was the absence, in most instances, of all evidence of the site of the embolic area, due to the sterile embolus when the lung was examined in the deflated state. Usually, but not always, inflation to a normal degree of 10 mm. of mercury disclosed the location of the embolus by a slightly paler color of the surface of the lung distal to the embolus. The clinical importance of this observation is apparent when one considers that most pathologists examine the lung only in the deflated state, and undoubtedly many sterile embolic areas are therefore overlooked.

In a series of thirty-two animals that were killed more than four days after operation and that had received simultaneously one infected and one sterile embolus, hemorrhagic infarction and abscesses were produced by the infected embolus in all but four instances. In these four animals killed fifteen, twenty-four, twenty-seven and ninety days after the introduction of the emboli, there was evidence of an old hemorrhagic infarction which had undergone resolution and healing by fibrosis.

In the three animals that died within forty-eight hours after the introduction of the emboli, there occurred massive hemorrhagic consolidation of the lobe containing the infected embolus.

The thirty-two sterile emboli produced in all but two instances no more alteration in the pulmonary tissue than a slight edema and a slight hemorrhagic infiltration, and often there was no evidence that even these changes had occurred. In one animal, however, that received both an infected and a sterile embolus, there occurred not only an abscess about the infected embolus, but also a typical hemorrhagic infarction distal to the sterile embolus. Such an infarction was produced in other instances only by an infected embolus, and as this animal, in common with many other examples, showed a blood culture positive for all three organisms originally introduced in the infected embolus, we are justified in assuming that the embolic area became secondarily infected by organisms circulating in the blood stream. Similarly, in another animal, K 26, there occurred multiple abscesses, not only in the embolic area distal to the infected embolus, but also in the area distal to the sterile embolus, which presumably become secondarily infected by organisms circulating in the blood stream.

Acting on the observations made in these two instances, sixteen other animals received two sterile emboli each, followed at varying intervals by the intravenous injection of 1 cc. of a bacterial emulsion. In one animal (K 56), two sterile jugular emboli were introduced, followed immediately by an injection into the femoral vein of a thin bacterial emulsion of *Staphylococcus aureus*. At necropsy, twenty-two days later,

an abscess was found containing one of the sterile emboli, whereas the lung in the region of the second embolus remained unchanged.

It is an arresting fact that in spite of a definite bacteremia intentionally produced following the introduction of the sterile emboli, there occurred only this one example of lowered resistance in the region of the embolus, as demonstrated by the formation of an abscess. Presumably the double blood supply to the lungs (3 and 4) is partly responsible for this protection, the prompt dilatation of the bronchial artery providing an adequate blood supply to the area deprived of the normal filling of the pulmonary artery.

This dilatation of the bronchial artery is undoubtedly of considerable clinical significance with reference to the concentration of the defense forces of the body around the infected part of the lung, and may account for the extraordinary ability of the lung to overcome and combat the evil effects of an infected embolus. Not infrequently one is greatly surprised by the ability of the lung to withstand an infection and to recover completely in spite of extensive destruction of pulmonary tissue. It is significant that infection about the sterile embolus occurred only when the bacteria were injected almost simultaneously with the introduction of the jugular emboli.

In two other instances, the bacteria were injected just prior to the introduction of the emboli. One animal died of an extensive bronchopneumonia in all parts of the lung, including the embolic areas. In the second animal, a hemorrhagic consolidation with destruction of pulmonary tissue and abscess formation occurred in the right lower lobe, which contained both sterile emboli. Our experiments on this phase of the study have not been completed.

That the embolic area beyond a sterile embolus may become secondarily infected, resulting in the production of an intrapulmonary abscess, is of considerable clinical and scientific importance. A sterile embolus may reach the lung from a clean operative wound or from a spontaneously developed thrombosis in the peripheral venous system. Infection of the resulting embolic area may occur from several sources: (a) from a transient bacteremia, (b) by direct extension from an intra-bronchial infection and (c) by the lymphatics running through the area.

As an example of what may happen clinically, the two following occurrences in our laboratory are of more than passing interest.

ANIMAL K 59.—On February 25, an experimental cholecystectomy was performed on animal K 59, following which the abdominal wound became infected. Only a draining sinus remained on March 13, when an exploratory laparotomy was performed by students. Again the wound became infected.

Twenty-eight days later, in the presence of two abdominal wounds draining a small amount of pus, two sterile emboli were introduced into the jugular vein. Pus continued to drain from the wounds until the animal was killed twenty-two days later. At necropsy, with the lung in the deflated state (fig. 8), a small scar

was found on the pleura of the left lower lobe, underneath which a round firm area, 1.5 cm. in diameter, could be felt. In the same lobe a second smaller, rounded, firm area could be felt. After inflation, the lung appeared remarkably different (fig. 8). There was marked retraction of the left lower lobe with marked diminution in its volume. It is evident that the true pathologic state of a lung cannot be determined by examination of the deflated lung only.

A roentgenogram showed both emboli in this left lower lobe with marked reaction about one of them. The bronchial artery leading to both emboli was markedly dilated, and the pulmonary artery beyond the emboli was not filled except for a slight injection in the region of the abscess through the bronchial artery (fig. 9).

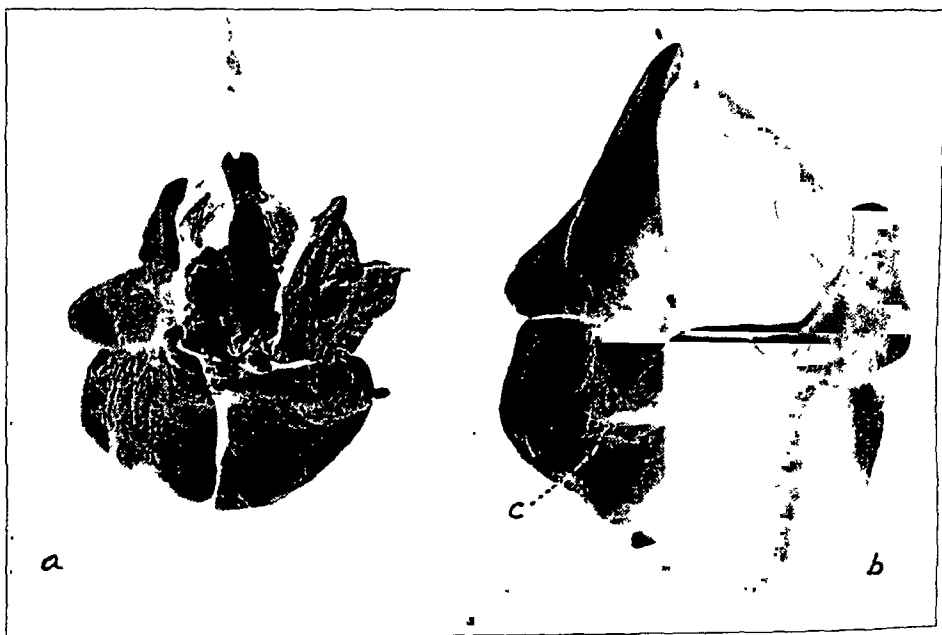


Fig. 8 (animal K 59).—Appearance of the uninflated lung (*a*) and the inflated lung (*b*) under a pressure of 10 mm. of mercury, showing the marked difference in the appearance of the lobes; *c*, abscess with marked retraction of the lobe in the region beyond a sterile embolus secondarily infected from an infected abdominal wound.

The cut section revealed a small irregular abscess cavity in which lay an embolus. Surrounding the cavity and extending to the visible depressed scar on the surface, there was a well defined area of consolidation. The second embolus was encapsulated by fibrous tissue, but otherwise there was no pathologic change in the pulmonary tissue around it.

ANIMAL R 49.—This animal was received at the laboratory with a compound suppurating fracture of the left hind leg. Aside from the open wound of the leg, the dog seemed well. On March 7, two sterile emboli were introduced into the jugular vein. The dog was killed eight days later, and at necropsy there was noted on the surface of the left upper lobe a deep red, softened area about

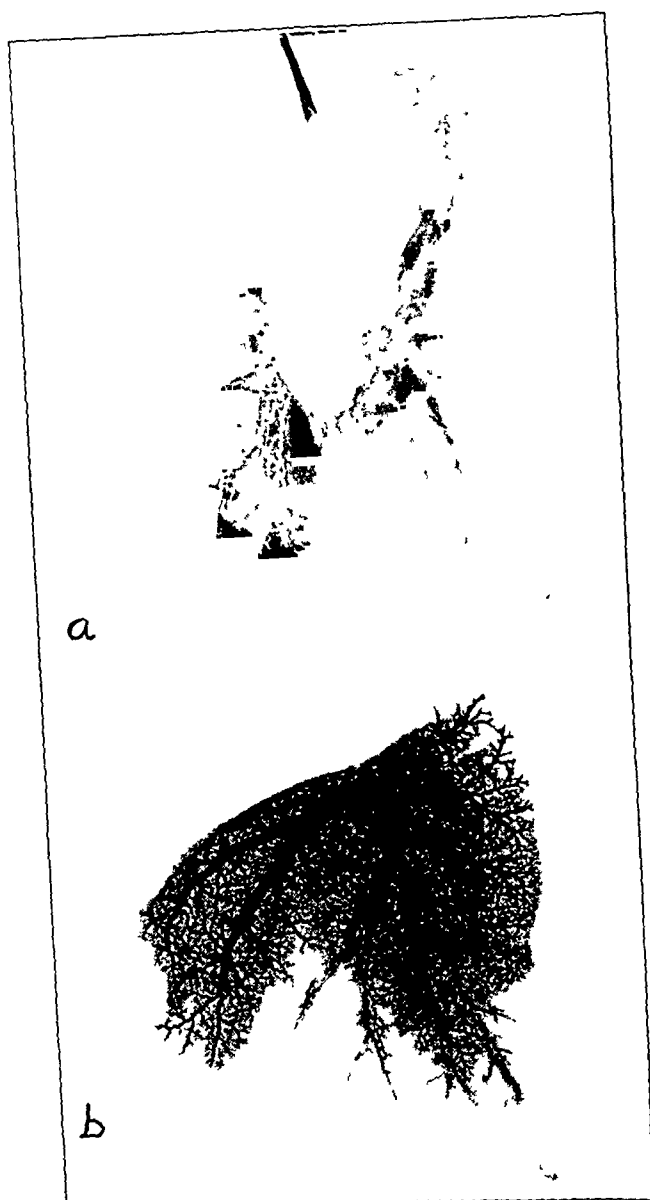


Fig. 9 (animal K 59).—*a*, injection of the bronchial artery showing marked dilatation leading to sterile emboli lodged in the same lobe, and slight filling of the pulmonary artery from the bronchial artery; *b*, injection of the pulmonary artery of the isolated lobe showing the absence of filling beyond the emboli except that due to the bronchial artery. The abscess produced in the area beyond one sterile embolus, due to secondary infection from a suppurating abdominal wound, is shown in fig. 8.



Fig. 10 (animal K 49).—*a*, injection of the bronchial artery in the presence of two sterile emboli, one secondarily infected from compound fracture sustained before the introduction of jugular emboli; *b*, lobe containing abscess; *c*, cut section of lobe containing the abscess; *d*, cut section of the lobe containing the second sterile embolus without reaction about it. Note the dilatation of the bronchial artery leading to the lobes containing the emboli.

2 cm. in diameter. The second embolic area was not visible until the lung was inflated, when it was disclosed in the right lower lobe by its paler color. The branches of the bronchial artery leading to the lobes that contained the emboli were greatly dilated, and there was no filling of the pulmonary artery beyond either embolus (fig. 10).

The cut section of the left upper lobe showed an abscess cavity, 1.5 cm. in diameter, with a fairly thick wall surrounded by a limited pneumonitis. There was no pathologic change around the second embolus.

SUMMARY

1. Experimental evidence is presented indicating that infected emboli invariably produce marked pathologic changes in the parenchyma of a lung.

2. Sterile emboli, on the other hand, usually produce little gross evidence of their presence in the deflated state of the lung. When the lung is expanded by normal inflation, the sterile embolic area is paler than the surrounding lung. Clinically, pathologists would do well to examine all lungs in the normally inflated state to aid in the detection of sterile embolic areas.

3. Sterile emboli may produce hemorrhagic infarction and abscess formation due to secondary infection of the embolic area by circulating organisms.

4. Observations in the laboratory indicate that in the presence of suppurating wounds a sterile embolus lodged in the lung may produce an intrapulmonary abscess due to secondary infection of the embolic area by circulating organisms.

5. The injection of the bronchial artery by the introduction of Hill's mass shows a marked dilatation of the branches leading to the lobes containing the emboli, more marked in the lobe containing the infected embolus. This dilatation of the bronchial artery may be of considerable clinical importance in the resistance to infection and in the repair of destroyed tissue following embolic infarction and abscess formation.

6. The injection of the pulmonary artery may be normal in the presence of massive hemorrhagic consolidation which may occur without an embolus or thrombosis in the pulmonary artery. Retrograde thrombosis does not explain the hemorrhagic consolidation following the lodging of an infected embolus in a lobe.

BRONCHOGENIC CONTAMINATION IN EMBOLIC ABSCCESS OF THE LUNGS*

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The etiology of abscess of the lung, particularly that which occurs after surgical operations, has been subject to recent clinical and experimental investigation, and much of pertinent data has been revealed. In the interpretation of this, difference of opinion has arisen as to whether inoculation of the lung occurs by aspiration of infectious material from the mouth or by embolism from an infected surgical wound. In favor of each has been presented a mass of clinical facts, and it must be admitted that most of these facts can be used equally effectively on either side of the argument. Also, experimentally, it has been possible to reproduce abscess of the lung by either portal of inoculation in substantiation. The aspiration theory has, however, been adopted by the majority as the more plausible. A critical review of the situation readily demonstrates essential defects in both explanations when applied to the etiology of typical postoperative abscess of the lung thus:

For many years pathologists have recognized that abscess of the lung may, on occasion, be produced either by septic embolism or by aspiration. A common observation after death in cases of pyemia is single or multiple acute pulmonary abscess, and the same organism is recovered from the lesion as from the primary infective focus. Also, massive aspiration of infectious material, particularly in the terminal stages of wasting diseases, is well known to give rise to bronchopneumonia, and there may be areas of softening. Here the outstanding circumstances are depleted resistance and overwhelming bacterial inoculation.

It is recognized¹ that embolism of major and minor proportions occasionally occurs following surgical operations, and the embolus is usually a fragment of blood clot loosened and deposited in the venous

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stream from a thrombus near the operative field. Moreover, thrombosis occurs most readily in the presence of infection, and these emboli may be septic. Therefore, it is altogether probable that abscess of the lung does arise, on occasion, from embolism after operation; but that this mechanism of inoculation accounts for the majority of these lesions appears doubtful. It does not explain the occurrence of abscess after sterile operations, nor does it account for the lack of correspondence between the bacterial flora typical of chronic abscess and that of the operative wound.

The strongest argument for aspiration as the mode of origin of pulmonary abscess is the close similarity between the type of bacterium infecting the lesion and that of the upper respiratory passages. Lambert and Miller² took cultures from ten abscesses directly at the time of pneumotomy, and found anaerobic bacteria to predominate in all. Smith³ studied various types of chronic suppurative disease of the lung, and recovered organisms native to the oral cavity. Also, that aspiration of material from the pharynx into the bronchi takes place with great frequency is abundantly demonstrated. Daily and Daily⁴ examined the tracheobronchial tree of 100 patients after tonsillectomy with general anesthesia, and found blood in seventy-eight. In a similar study, Myerson,⁵ showed bacterial contamination in 76 per cent, although he had tilted the head of the table downward at an angle of 45 degrees during the operation. Iglauer⁶ examined fifty patients after tonsillectomy under local anesthesia (procaine hydrochloride), and noted blood in the trachea in 38 per cent. In five of these, 5 cc. of iodized oil was given to be swallowed, and in two the oil entered the lower respiratory tract. Ochsner and Nesbit⁷ found that every patient with peritonsillar infiltration anesthesia and before tonsillectomy aspirated iodized oil in trying to swallow. Corper⁸ instilled india ink (2 cc.) into the nose of conscious, unanesthetized rabbits, and discovered that a large part of it was deposited in the lung; and similar experimental results in both anesthetized and unanesthetized animals are reported by others.⁹ That aspiration of pharyngeal fluids readily occurs in man without any

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9. Mullin, W. V., and Ryder, C. T.: *Am. Rev. Tuberc.* **4**:683, 1920. Corper, H. J., and Enright, J. J.: Eye as Portal of Infection in Respiratory Disease, *J. A. M. A.* **74**:521 (Feb. 21) 1920. Hoelscher, R.: *Arch. f. klin. Chir.* **57**:175, 1897. Lemon, W. S.: Aspiration, *Arch. Surg.* **12**:187 (Jan.) 1926.

form of anesthesia and unknown to the individual is known as a fact to those who are familiar with the Singer¹⁰ method for the introduction of iodized oil intrabronchially. The patient is seated, the tongue is steadied and the oil is instilled into the pharynx. If swallowing is forbidden, the oil runs into the larynx, trachea and bronchi freely and without sensation. Myerson¹¹ draws the pertinent conclusion that bland substances, such as mucus, saliva, blood, etc., and others, when well mixed with mucus, do not stimulate the mucosa of the larynx and lower respiratory tract sufficiently to excite cough. Only when the mass of aspirated material is sufficient to interfere with the passage of air or when the mucosa is hyperirritable and inflamed, is the cough reflex called into play.

This fact of frequent contamination of the lower respiratory tract from the upper is, indeed, the strongest argument against the aspiration hypothesis of the origin of abscess of the lung. That lesion is rare. Moore¹² reported one abscess of the lung in 3,000 tonsillectomies; Graham¹³ found no abscess in 10,000 (material from Sluder's clinic). The answer to this difficulty has been that the aspirated substance is regularly and quickly eliminated by cough, ciliary activity and bronchial peristalsis. Myerson¹⁴ observed directly in man an evacuation time of twelve minutes, even under anesthesia and without cough! It is suggested¹⁵ that in certain persons this mechanism of elimination fails, and from prolonged contact of the inoculum with the finer ramifications of the bronchi, infection of the parenchyma occurs. But fluid, even in small quantity and when not too viscid, introduced into the trachea, gravitates immediately to the periphery of the lung where it is beyond the expelling reach of cough and ciliary activity. Thus, Hoelscher¹⁶ stained the buccal secretions in anesthetized dogs and found the alveoli of the lung to become stained, and Mullin and Ryder¹⁷ noted the same condition in rabbits. Corper⁸ found that particles of india ink aspirated from the pharynx reached the alveoli and remained there as long as three months. In man, after intrabronchial injection of iodized oil, it is common to see the oil reach the finest bronchioles or alveoli and remain

10. Singer, J. J.: Bronchography: Injection of Iodized Oil, *Arch. Surg.* **14**:167 (Jan.) 1927.

11. Myerson (footnote 5, second reference).

12. Moore, W. F.: Pulmonary Abscess, *J. A. M. A.* **78**:1279 (April) 1922.

13. Graham, E. A.: *S. Clin. N. Amer.* **2**:1501, 1922.

14. Myerson (footnote 5, first reference).

15. Hedblom, C. A.; Joannides, M., and Rosenthal, S.: *Ann. Surg.* **88**:823, 1928. Allen, D. S.: Etiology of Abscess of the Lung: Experimental and Clinical Studies, *Arch. Surg.* **16**:179 (Jan.) 1928.

16. Hoelscher (footnote 9, third reference).

17. Mullin and Ryder (footnote 9, first reference).

there for months, as shown by fluffy shadows in x-ray films. Archibald¹⁸ found that when substances were aspirated below a certain zone in the bronchial tree, cough had the effect of driving them further toward the periphery.

The proponents of the aspiration hypothesis also assume coincidentally lowered resistance of the host. This is undoubtedly important, but difficulties arise at once. Thus, a recent autopsy at this institution demonstrated a carcinoma of the esophagus. A fistula had developed between the esophagus and the bronchus, which had permitted massive, daily bronchial contamination. The fistulous tract swarmed with fusospirochetes and other putrefying bacteria. The patient was aged and extremely cachectic. Bronchopneumonia was present but no abscess. Moreover, statistics¹⁹ show that the lowest incidence of post-operative pulmonary complications of all sorts is seen in operations on the brain, and here the patient is frequently submitted to severest shock and hours of deep unconsciousness and depression. Indeed, the circumstances responsible for the greatest number of abscesses of the lung are quite the opposite, i.e., those of tonsillectomy, a minor operation performed on relatively young and healthy persons. If lowered resistance of the host plays an essential rôle, it is specific and not yet understood.

Animal researches in the reproduction of abscess of the lung have corroborated these conclusions, but add little. Regarding embolic inoculation, it has been shown²⁰ that infected emboli reaching the lung readily give rise to an abscess. If the infecting agent is one of the ordinary pus formers, as *Staphylococcus aureus*, the abscess is insignificant and heals quickly, but if more virulent and anaerobic pyogens are used, such as are native to the mouth, the abscess is usually larger and tends to become chronic.²¹ On the other hand, intrabronchial inoculation has produced abscess of the lung with excessive difficulty. Lambert and Miller,² Aschner,²² Cutler and Schlueter,²⁰ Schlueter and Weidlein,²³ and many others have insufflated or packed the bronchi with a variety of infectious materials in hundreds of animals, and produced either

18. Archibald, E., and Brown, A. L.: Am. Rev. Tuberc. **16**:111, 1927.

19. Cutler, E. C., and Hunt, A. M.: Postoperative Pulmonary Complications, Arch. Surg. **1**:114 (July) 1920.

20. Cutler, E. C., and Schlueter, S. A.: Ann. Surg. **84**:256, 1926. Holman, E.; Weidlein, I. F., and Schlueter, S. A.: Proc. Soc. Exper. Biol. & Med. **23**:266, 1926.

21. Hermann, L. G., and Cutler, E. C.: Proc. Soc. Exper. Biol. & Med. **26**:28, 1928.

22. Aschner, P. W.: Ann. Surg. **75**:321, 1922.

23. Schlueter, S. A., and Weidlein, I. F.: Postoperative Lung Abscess: Experimental Study, Arch. Surg. **14**:457 (Feb.) 1927.

bronchopneumonia, septicemia or no lesion. Similarly, Allen²⁴ recently failed to produce abscess of the lung, after insufflating pus from a pulmonary abscess in man into the bronchi of fifteen rats and fifteen dogs. He then modified the experiment by ligating the insufflated bronchus, in order to retain the inoculum in contact with the lung. The lesions thus obtained were termed abscesses, but they are described and illustrated as purulent, desquamative bronchitis and peribronchial leukocytic infiltration, i.e., bronchopneumonia. No protocols are published describing tissue necrosis and cavity formation, which are necessary characteristics of abscess in any part.

Intrabronchial inoculation has succeeded, however, in producing destructive lesions of the lung in animals, and here a specific organism appears to have been a constant factor, viz., the fusospirochete of Vincent. Smith²⁵ instilled warm, fresh suspensions of these organisms, obtained from scrapings of carious teeth in man, into the bronchi of rats, guinea-pigs and rabbits. Bronchopneumonia resulted with central necrosis, and chronic abscesses persisted in some cases for five months.²⁵ Crowe and Scarff, after working two years with infective agents, succeeded in obtaining abscess of the lung in nine dogs with Vincent's fusospirochetes. In eight of these, the entire lobe inoculated became gangrenous. Following them, Hedblom, Joannides and Rosenthal²⁶ insufflated the bronchial tree of sixty-seven dogs with a wide assortment of infectious and irritating substances. Unfortunately, little detail is given, but the inference is apparent that abscesses were obtained when fusospirochetes were included in the inoculum, and these authors emphasize the importance of this group of organisms to the production of abscess. The lesion produced, as far as described, was pulmonary gangrene. In three dogs, the inoculated lobe was partially or wholly gangrenous, and in one the "abscess" measured 10 cm. in diameter, which means a widespread destruction of substance of the lung.

These experiments have, accordingly, given rise to a specific lesion, pulmonary gangrene. The work supports the original, extensive investigations of Pilot,²⁷ Pilot and Davis,²⁸ Pilot, Davis and Shapiro,²⁹ and Kline,³⁰ showing that the Vincent group of anaerobic bacteria have

24. Allen (footnote 15, second reference).

25. Smith, D. T.: *Am. Rev. Tuberc.* **16**:584, 1927.

26. Hedblom; Joannides, and Rosenthal (footnote 15, first reference).

27. Pilot, I.: *S. Clin. N. Amer.* **9**:1433, 1926.

28. Pilot, I., and Davis, D. J.: *Studies in Fusiform Bacilli and Spirochetes: Their Rôle in Pulmonary Abscess, Gangrene and Bronchiectasis*, *Arch. Int. Med.* **34**:313 (Sept.) 1924.

29. Pilot, I.; Davis, D. J., and Shapiro, I. J.: *Am. Rev. Tuberc.* **8**:249, 1923.

30. Kline, B. S.: *Spirochetal Pulmonary Gangrene*, *J. A. M. A.* **77**:1874 (Dec. 10) 1921; *J. Infect. Dis.* **32**:481, 1923.

the capacity to necrotize and putrefy tissues; but that it furthers the question of etiology of the typical chronic abscess of the lung in man is doubtful. Pulmonary gangrene not infrequently complicates abscess of the lung, but it is in itself a distinct pathologic and bacteriologic entity. Characteristically, gangrene is acute and lacking in protective tissue reaction, while abscess may be acute or chronic and tends from the start to encapsulation. Gangrene presents a foul, penetrating odor and a bacterial flora that is putrefactive and often includes Vincent organisms; chronic abscess of the lung frequently has little odor and a mixed, largely anaerobic bacterial flora frequently including putrefying bacteria. Smith³¹ studied the bacteriology of bronchopulmonary spirochetosis as reported and in cases of his own, and found included all types of suppurative disease of the lung, including abscess; following his work writers have tended to consider fusospirochetes as characteristic of abscess of the lung. Smith, however, did not demonstrate the corollary, i. e., that suppurative diseases of the lung, including abscess, are regularly due to fusospirochetes. Lambert and Miller² found these organisms in 30 per cent of abscesses from which cultures were taken directly. Fusospirochetes occasionally appear in lesions of the lower respiratory tract, just as they are seen at times in lesions of the tracts above the larynx. And it is as unreasonable to consider them the essential cause of abscess of the lung, as it would be to suggest that all tonsillitis, sinusitis or dental caries are caused by them, since they frequent these lesions. Nor would inoculation experiments, injecting fusospirochetes into the tonsils or sinuses of dogs and producing specific tissue putrefaction, show that tonsillitis or sinusitis occurs spontaneously from these organisms and in this manner. Surely, massive doses of such necrotizing bacteria blown into a bronchus in man would often give rise to gangrene of the lung, but these are clearly not the circumstances usually attending the onset of pulmonary abscess.

In short, both clinical and laboratory experience demonstrate the lung to be very susceptible to abscess formation from septic embolism and very resistant in this respect to bronchogenic inoculation, when bacteria are used which are common to chronic abscess of the lung. While certain abscesses of the lung in man doubtless result from embolic origin alone and others from a bronchogenic source, there remains a large group of postoperative pulmonary abscesses, which are not readily explained by either mode of origin.

For these cases we wish to suggest a combination of these two factors, where embolism contributes the initial acute abscess and aspiration changes the flora to that of the upper respiratory passages and con-

31. Smith (footnotes 3 and 25).

tributes toxicity and chronicity to the lesion. The experiments that follow are planned to test the possibility of this in animals.

EXPERIMENTAL WORK

Dogs were used, and were divided into three groups. In group 1 the effect of insufflation alone of infectious material into the bronchus was determined. In group 2 the nature of the abscess produced by embolic inoculation alone of the lung was defined. And in group 3 the change that may be effected in the character of embolic abscess of the lung as result of septic bronchial insufflation was determined.

Various types of bacteria were employed for inoculation, for the purpose of contrasting the action of a common pyogenic organism, *Staphylococcus aureus*, with that of bacteria of greater virulence, in mixture and sort as found in chronic suppurative diseases of the lung.

GROUP 1.—In this group, the effect of intrabronchial insufflation alone was determined on twenty-two dogs. The dogs were anesthetized to the extent of

TABLE 1.—*Intrabronchial Insufflation with Sputum Containing Vincent's Fusospirochetes*

Number of Dogs	Spontaneous Deaths		Killed	
	Day	Abscess	Day	Abscess
16	1	None	12	None
	1	None		None
	1	None		None
	2	None		None
	4	None		None
	4	None		None
				None
				None
				None

deep sleep and loss of cough reflex for eighteen to twenty-four hours by subcutaneous injection of sodium barbital, 0.3 Gm. per kilogram of body weight. Sputum was obtained absolutely fresh, thinned with saline to lower its viscosity, and insufflated bronchoscopically into the right lower bronchus in amounts of 0.3 cc. per kilogram of body weight. Afterward, the animals were placed to sleep on the right side with the head elevated to insure retention of the inoculum in the bronchus. The subsequent behavior was noted. At death from disease or when killed after selected intervals, autopsy was done including the gross and microscopic pathologic and bacteriologic examinations of the lungs. The results of the gross pathologic examination only will be reported here as directly pertinent, and the other results will appear in subsequent publications.

Series A, sixteen dogs: Sputum containing myriads of fusospirochetes of Vincent, cocci and rods, taken from a case of bronchiectasis, was insufflated into the dogs (table 1). Six of them died in four days with pulmonary congestion, pneumonia and toxemia. Ten were killed in twelve days. Bronchitis was the only lesion found.

Series B, six dogs: Sputum containing *Fungus nocardia*, cocci and rods, obtained from a case of bronchiectatic abscess of the lung, was insufflated (table 2). Four dogs died on the second day with pulmonary congestion and toxemia. Two killed in eleven days showed bronchitis only.

GROUP 2.—In this group the effect of embolic inoculation of the lung alone was determined on fifty-four dogs.

An embolus was prepared after the method of Cutler, Holman and their associates; i. e., into the lumen of a short segment of femoral vein was placed the infectious material (fragment of cotton saturated with sputum or a piece of agar-bearing bacterial culture) and a lead bird-shot. The ends of the vein were then tied with linen thread to retain the contents. The dog to be inoculated was anesthetized with ether; an incision was made exposing the external jugular vein, and the embolus was introduced into its venous blood stream. The after-management was the same as for group 1.

TABLE 2.—Intrabronchial Insufflation with Sputum Containing Fungus *Nocardia*

Number of Dogs	Spontaneous Deaths		Killed	
	Day	Abscess	Day	Abscess
6	2	None None None None	11	None None

TABLE 3.—Embolic Inoculation of the Lung with Sputum Containing Fungus *Nocardia*

Number of Dogs	Spontaneous Deaths		Killed	
	Day	Abscess	Day	Abscess
5	30	Healed Large Large Large Large

TABLE 4.—Embolic Inoculation of the Lung with Sputum Containing Mixed Pyogenic Organisms

Number of Dogs	Spontaneous Deaths		Killed	
	Day	Abscess	Day	Abscess
6	6	Gangrene	63	Large Large Large Large Very large

Series A, five dogs: An embolus infected with sputum containing *Fungus nocardia*, cocci and rods, obtained from a case of bronchiectatic abscess of the lung (group 1, B), was introduced (table 3). All dogs were killed in thirty days. One showed the lead pellet encapsulated in fibrous tissue in the parenchyma of the lung and no abscess. Four presented a large abscess at the site of the embolus. The walls of the abscess were soft, and the cavity contained purulent material and the remains of the embolus. The surrounding lung was more or less consolidated with active inflammatory reaction. The bronchi contained mucopurulent secretion and were injected.

Series B, six dogs: An embolus infected with sputum containing mixed pyogenic cocci and rods and without specific bacteria, obtained from a case of postpneumonic abscess of the lung, was introduced (table 4). One dog died on

the sixth day with extensive gangrene of the left upper lobe of the lung, lying in a pyramidal area distal to a small abscess containing the embolus. Both pleural cavities contained purulent fluid. Five dogs were killed in sixty-three days, and all showed a large abscess at the embolus. These differed on the whole from those in series A in that their walls were more fibrous, less débris was in the cavities and the surrounding parenchyma was less inflamed.

Series C, twenty-six dogs: An embolus infected with sputum containing a mixture of pyogenic cocci and rods and without specific bacteria, obtained from a case of bronchiectasis, was introduced (table 5). Twelve dogs died; six of these died in six days with pulmonary congestion, pneumonia and general toxemia; and six in from nine to seventeen days, three with distemper and three from the effects of a large acute abscess of the lung at the embolic focus. Eight were killed in sixty-four days. Seven showed the embolus encapsulated in scarred parenchyma of the lung, and one had a large abscess similar to those described in the previous series. One was killed in ninety-one days and presented a large chronic abscess of the lung (fig. 1). Five were killed in 119 days. In one there

TABLE 5.—*Embolic Inoculation of the Lung with Sputum Containing Mixed Pyogenic Organisms*

Number of Dogs	Spontaneous Deaths		Killed					
	Day	Abscess	Day	Abscess	Day	Abscess	Day	Abscess
26	2	None	64	Healed	91	Large	119	None
	3	None		Healed				Healed
	3	None		Healed				Healed
	5	None		Healed				Large
	6	None		Healed				Large
	6	None		Healed				
	9	Large		Healed				
	9	Large		Large				
	10	None						
	13	Large						
	15	None						
	17	None						

had apparently been no abscess, for the embolus was contained in intact arterial walls; in two the abscess was healed, for the embolus was embedded in scar; and in two there was a large abscess. This was represented by a cavity with fibrous walls, no contents, a smooth surface and without surrounding pneumonia (fig. 2).

Series D, seventeen dogs: An embolus infected with blood agar culture of *Staphylococcus aureus*, of known virulence in man, twenty-four hours old, was introduced (table 6). Three dogs died of distemper in from fourteen to twenty-two days; two of these had an healed abscess and the other had a very small abscess cavity a trifle larger than the bird-shot it contained. Fourteen were killed in thirty days. In two there was a small abscess of the lung nearly healed, and in the others evidence of healed abscess was found, or no inflammatory reaction at all at the site of the embolus.

GROUP 3.—In this group the effect of embolic inoculation of the lung, plus intrabronchial inoculation, was determined on sixty-eight dogs.

Pulmonary embolism was induced, as in group 2, and on the tenth day the position of the embolus in the lung was localized by the x-rays, and the bronchus to that part was inoculated, as in group 1. In each case, the embolus carried *Staphylococcus aureus* (group 2, D). For insufflation, sputum was used from the cases in the foregoing experiments, also *Staphylococcus aureus* alone and sterilized sputum alone.

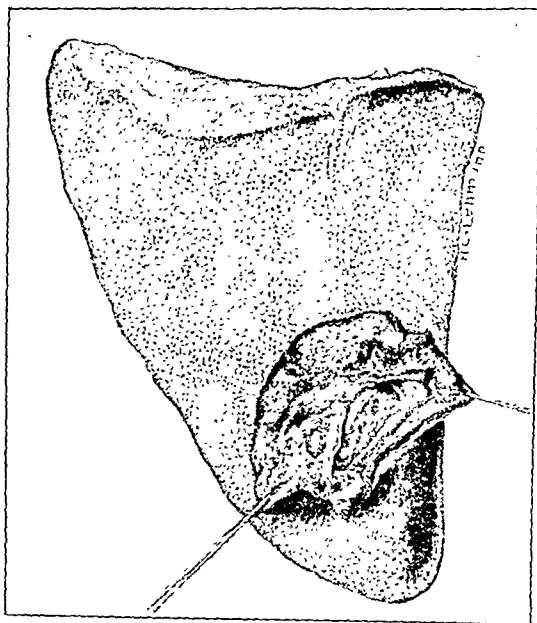


Fig. 1.—Right lower lobe of the lung, incised to show abscess ninety-one days after embolic inoculation with sputum containing a mixture of pyogenic cocci and rods (no specific bacteria). See group 2, series C.

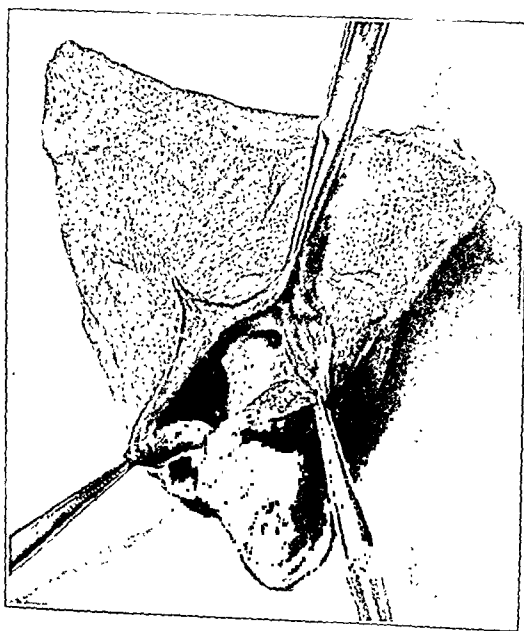


Fig. 2.—Right lower lobe of the lung, incised to show abscess 119 days after embolic inoculation with sputum containing a mixture of pyogenic cocci and rods (no specific bacteria). See group 2, series C.

Series A, eight dogs: An embolus infected with *Staphylococcus aureus* was introduced, and sputum containing fusospirochetes of Vincent, cocci and rods, obtained from a case of bronchiectasis (group 1, A), was insufflated (table 7). Two dogs died in twelve days from the effects of large acute abscess and the toxemia of insufflation (fig. 3). Six dogs were killed in thirty-four days, and all showed a large abscess at the embolic site. This contained pus and débris, and the surrounding lung was consolidated.

TABLE 6.—*Embolic Inoculation of the Lung with Agar Culture of Staphylococcus Aureus*

Number of Dogs	Spontaneous Deaths		Killed	
	Day	Abscess	Day	Abscess
17	14	Small	30	None
	21	Healed		None
	22	Healed		None
				Healed
				Healed
				Healed
				Healed
				Healed
				Healed
				Healed
				Healed
				Small
				Small

TABLE 7.—*Embolic Inoculation of the Lung with Staphylococcus Aureus Plus Intrabronchial Insufflation with Sputum Containing Vincent's Fusospirochetes*

Number of Dogs	Spontaneous Deaths		Killed	
	Day	Abscess	Day	Abscess
8	12	Large	34	Large
		Large		Large
		Large		Large
				Large
				Large
				Large

TABLE 8.—*Embolic Inoculation of the Lung with Staphylococcus Aureus Plus Intrabronchial Insufflation with Sputum Containing Fungus Nocardia*

Number of Dogs	Spontaneous Deaths		Killed	
	Day	Abscess	Day	Abscess
6	1	None	30	Healed
	11	Small		Healed
	11	Small		Large

Series B, six dogs: An embolus infected with *Staphylococcus aureus* was introduced, and sputum, containing *Fungus nocardia*, cocci and rods, obtained from a case of bronchiectatic abscess of the lung (group 1, B and group 2, A) was insufflated (table 8). Three dogs died; one of these died after twenty-four hours from unknown causes, and two died in eleven days as the result of the toxemia of insufflation. Each of the latter presented small acute abscess of the lung. Three dogs were killed in thirty days; two of these had an healed abscess, and one had a large acute abscess containing the embolus.

Series C, eighteen dogs: An embolus infected with *Staphylococcus aureus* was introduced, and sputum containing mixed pyogenic cocci and rods and no specific bacteria, obtained from a case of bronchiectasis (group 2, C), was insufflated (table 9). Six dogs died in from three to ten days; four with pulmonary congestion and toxemia, and two with distemper. Three showed a small abscess at the site of embolism. Five were killed in sixty-two days. Of these, three had an healed abscess, one a small, active abscess, and one a very large, chronic abscess. Seven were killed in ninety-three days. Five had an healed abscess and two a large abscess. One of the latter abscesses was of the indolent type with

TABLE 9.—*Embolic Inoculation of the Lung with Staphylococcus Aureus Plus Intrabronchial Insufflation with Sputum Containing Mixed Pyogenic Organisms*

Number of Dogs	Spontaneous Deaths		Killed			
	Day	Abscess	Day	Abscess	Day	Abscess
18	3	None	62	Healed	93	Healed
	3	None		Healed		Healed
	6	None		Healed		Healed
	8	Small		Small		Healed
	10	Small		Large		Healed
	10	Small				Large

TABLE 10.—*Embolic Inoculation of the Lung with Staphylococcus Aureus Plus Intrabronchial Insufflation with Staphylococcus Aureus*

Number of Dogs	Spontaneous Deaths		Killed			
	Day	Abscess	Day	Abscess	Day	Abscess
27	1	None	30	Healed	61	None
	2	None		Healed		None
	2	None		Healed		Healed
	2	None		Small		Healed
	3	Small		Large		Healed
	4	Large				Small
	7	None				Small
	8	None				Small
	9	Small				
	9	Large				
	11	None				
	11	None				
	12	None				
	23	Healed				

little remaining inflammation (fig. 4). The other had a multilocular cavity, filled with thick pus, and the adjacent lung was widely consolidated.

Series D, twenty-seven dogs: An embolus infected with *Staphylococcus aureus* was introduced, and *Staphylococcus aureus* in twenty-four hour broth culture was insufflated (table 10). Fourteen dogs died within twenty-eight days from an epidemic of distemper that decimated the stock at this time. Four of these had an embolic abscess, two small, one medium and one large. Five dogs were killed in thirty days; three had an healed abscess, one a very small, inactive abscess, and one a large abscess filled with purulent material. Eight were killed in sixty-one days, and three of these showed a small, nearly healed abscess at the embolic site.

Series E, nine dogs: An embolus infected with *Staphylococcus aureus* was introduced, and sterilized sputum was insufflated (table 11). Three dogs died in seven days, with pulmonary congestion and toxemia. No abscesses were found

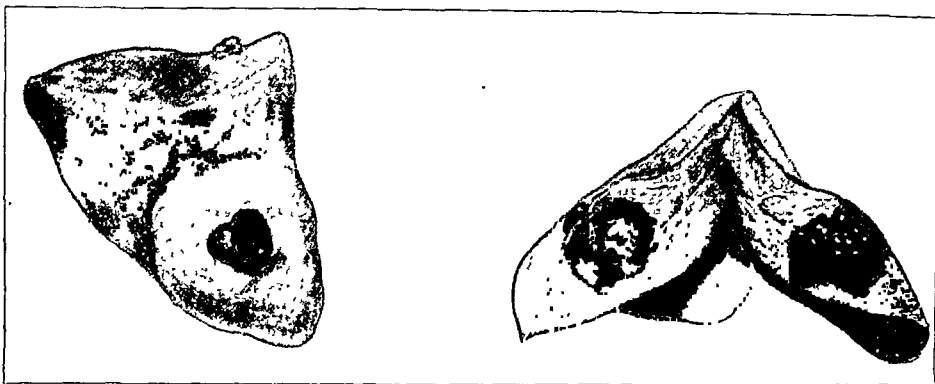


Fig. 3.—Left lower lobe of the lung showing abscess twelve days after embolic inoculation with *Staphylococcus aureus* and two days after intrabronchial insufflation with sputum containing fusospirochetes of Vincent. See group 3, series A.

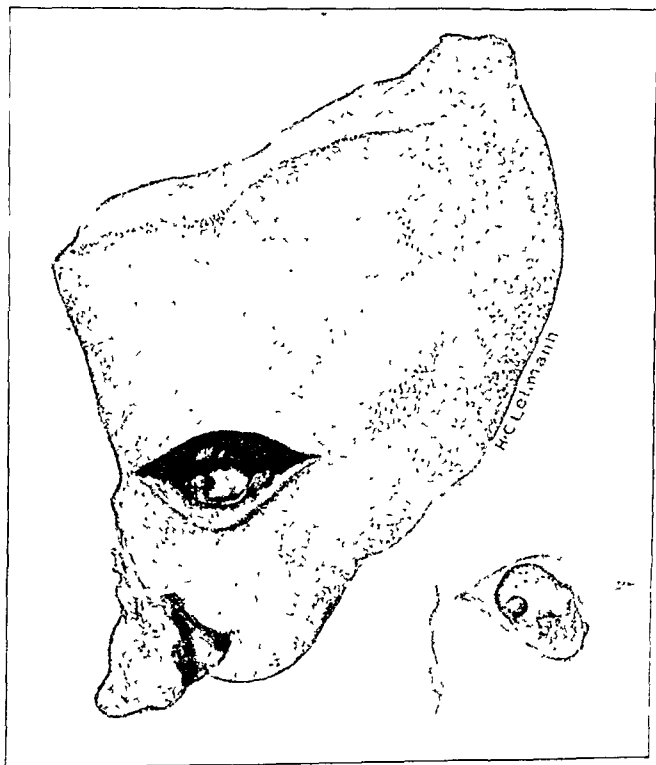


Fig. 4.—Left lower lobe of the lung showing abscess ninety-three days after embolic inoculation with *Staphylococcus aureus* and eighty-three days after intrabronchial insufflation with sputum containing mixed pyogenic cocci and rods (no specific bacteria). See group 3, series C.

and the emboli were contained in intact arterial walls. Six were killed in thirty-one days. In five there was evidence of healed abscess, and in one apparently no abscess had existed.

Summary of Results.—The experiments include 144 dogs, divided into three groups (table 12).

Group 1, twenty-two dogs, received only intrabronchial insufflation of sputum from cases of chronic suppurative pulmonary disease. The mortality, 45 per cent, was from pneumonia, empyema and toxemia. No abscess of the lung developed.

TABLE 11.—*Embolie Inoculation of the Lung with Staphylococcus Aureus Plus Intrabronchial Insufflation with Sterile Sputum*

Number of Dogs	Spontaneous Deaths		Killed	
	Day	Abscess	Day	Abscess
9	1	None	31	None
	4	None		Healed
	7	None		Healed
				Healed
				Healed

TABLE 12.—*Summary*

Group	Method of Inoculation	Inoculum	Number of Dogs	Per Cent Survived	Per Cent With Abscess Active			
					1 Mo.	2 Mo.	3 Mo.	4 Mo.
1	Insufflation	Sputum	22	55	0			
2	Production of embolism	(1) Sputum	37	65	54	47	50	40
		(2) <i>Staphylococcus aureus</i>	17	82	14			
3	Production of embolism plus insufflation	<i>Staphylococcus aureus</i>						
		(1) Sputum	32	66	52	33	29	
		(2) <i>Staphylococcus aureus</i>	27	45	39	37		
		(3) Sterile sputum	9	66	0			

Group 2, fifty-four dogs, received only infected emboli. In a part of these the embolus was infected by sputum, and in the remainder by *Staphylococcus aureus* culture. The mortality was 29 per cent. Of those inoculated with sputum and surviving, 54 per cent had abscess of the lung unhealed at one month, 47 per cent unhealed at two months, 50 per cent unhealed at three months, and 40 per cent at four months. Of those inoculated with *Staphylococcus aureus* and surviving, 14 per cent had abscess of the lung at one month, and these were small and nearly healed.

Group 3, sixty-eight dogs, received embolic inoculation of the lung with *Staphylococcus aureus* and, ten days later, intrabronchial insufflation of various inocula. The mortality was 41 per cent. In a part of the dogs, sputum was insufflated, and of the survivors, 52 per cent had an

abscess of the lung unhealed at one month, 33 per cent unhealed at two months, and 29 per cent unhealed at three months. In a second part, *Staphylococcus aureus* culture was insufflated, and of those surviving, 39 per cent had unhealed abscess at one month and 37 per cent at two months. In a third part, sterilized sputum was insufflated and no abscess remained to one month.

COMMENT AND CONCLUSIONS

The first two groups of experiments determine the mode of reaction of the lung separately to embolic and bronchogenic inoculation, and serve as controls for the third group. Two phenomena are illustrated thereby that we have already referred to from the work of others, but which deserve emphasis.

Thus, first, the lung is far more susceptible to abscess formation from embolic than from bronchogenic inoculation. This is of importance in the question of etiology of abscess of the lung, and further study has been made of its nature and causes.³²

Second, these experiments demonstrate a direct relation between the type of organism infecting an embolic abscess of the lung and the virulence and chronicity of the abscess. Accordingly, *Staphylococcus aureus* alone produced small abscesses which tended to heal in a few weeks, while mixtures of pyogenic bacteria, such as exist in the sputum of chronic suppurative pulmonary diseases (nontuberculous), evolved large abscesses that often required months for healing. We disagree with recent authors who claim a specificity of fusospirochetes of Vincent for the production of chronic abscess of the lung. Experimentally, at least, the common pyogenic cocci and rods of sputum are as capable of inducing abscesses slow to heal as are spirochetes.³³

Group 3 indicates the effect that intrabronchial contamination may have on the character of a preexisting abscess of the lung. Here the abscess was initiated by an embolus carrying a type of bacterium (*Staphylococcus aureus*) that produces essentially insignificant and rapidly healing abscesses. Insufflation of sputum organisms was carried out on the tenth day. The virulence and chronicity of the abscess were found to be enhanced to a degree similar to that characteristic of abscess of the lung initiated by sputum organisms. Secondary contamination of the abscess by way of the bronchi is believed to play an important rôle in production of this alteration.

We suggest a circumstance, as here, with initiation of the abscess by infected embolus and propagation by bronchogenic contamination, as

32. Van Allen, C. M.; Adams, W. E., and Hrdina, L. S.: Embolism in Bronchogenic Infection of the Lung, p. 1279 of this issue.

33. Van Allen, C. M.; Adams, W. E., and Hrdina, L. S., ready for publication.

pertaining to the pathogenesis of certain postoperative chronic abscesses of the lung in man, which we have referred to in the introduction as inadequately explained by supposing either mode of inoculation to act alone. This would account, in the embolic theory, for the disparity often existing between the bacterial flora of the abscess and that of the operative field; and, again, why abscess of the lung regularly contains organisms native to the mouth, in spite of the excessive difficulty with which these organisms, when introduced into the bronchus, produce abscess of the lung. Thus, the main obstacle of each hypothesis taken alone is removed by combining the two. This mode of origin corresponds, also, with the rarity of abscess of the lung as a postoperative complication, since postoperative embolism is unusual; only certain of the emboli carry organisms capable of forming abscess, and of the abscesses a part only would be expected to acquire communication with a bronchus to permit contamination.

In one series of dogs (group 3, D), a moderate but distinct increase in virulence and chronicity of *Staphylococcus aureus* abscess followed intrabronchial insufflation of the same organism. Other experiments are under way, in which the same organism is employed for insufflation as for embolism, and these show the same effect. Evidently, replenishment of the bacterial flora in the abscess can maintain it, as well as can alteration of the bacterial flora types. This probably explains reactivation of bronchiectasis that occurs during recrudescences of chronic paranasal sinusitis.³⁴ Superinoculation by aspiration accounts for the fact that postpneumonic abscess of the lung also is commonly infected with bacteria from the mouth.³

It has been pointed out in objection to the embolic origin of postoperative abscess of the lung that in many cases signs and symptoms of pulmonary embolism do not appear in the prodromal period. This is true, but one needs only to recall how frequent it is to see at autopsy small pulmonary infarcts, even acute embolic abscesses of the lung which have gone undiagnosed in the wards, to appreciate that minor embolism may occur without recognizable signs during life.

The theory of combined origin of postoperative abscess of the lung, as outlined here, fails to account for those abscesses which occur after a sterile operation. The explanation of this on a similar basis is considered in another communication.³²

SUMMARY

Attention was called to the fact that a large group of postoperative abscesses of the lung exists which is not adequately explained as to etiology either by embolic or by bronchogenic inoculation, acting alone.

34. Graham, E. A., in discussion on Lemon, W. S.: Aspiration, Arch. Surg. 12:187 (Jan.) 1926.

The effect of a combination of these two avenues of inoculation of the lung was tested experimentally.

It was found that embolic abscesses of the lung could be enhanced in virulence and chronicity by insufflation of infectious material into the bronchus. This combination of embolic and bronchogenic inoculation may explain the pathogenesis of the obscure group of postoperative abscesses of the lung. Superinoculation by aspiration of pharyngeal secretions may be responsible chiefly for the maintenance of chronic abscess of the lung, both postoperative and postpneumonic, and for recrudescences in bronchiectasis.

EMBOLISM IN BRONCHOGENIC INFECTION OF THE LUNG*

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In another publication¹ are described the effects on the lung of dogs produced by embolic and intrabronchial inoculation, employed separately and combined. It appeared that interaction of both of these portals of entry for organisms to the lung pertains to the pathogenesis of certain postoperative abscesses of the lung in man of obscure origin.

These experiments, moreover, emphasized the fact that abscess develops readily from embolic inoculation of the parenchyma of the lung, but with great difficulty, if at all, after intrabronchial implantation of the same infecting agents, although used in enormously larger quantity. This phenomenon is considered further in the present communication.

Others have called attention to the same circumstance. One explanation has been that embolism interferes with the blood supply of the part inoculated and lowers its resistance.² Another reason, more generally given,³ is that material deposited in the tracheobronchial tract is quickly removed by cough and ciliary activity, and invasion of the parenchyma is thus prevented. But the latter fails to consider the abundant clinical and experimental proof available that fluids, even in small amounts, deposited in the trachea gravitate readily to the terminal ramifications of the bronchial tree and tend to remain there beyond the reach of natural expelling forces.

The resistance of the lung to abscess formation from intrabronchial contamination is not due to failure of inoculation. It is well appreciated,⁴

* From the Department of Surgery, University of Chicago.

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1. Van Allen, C. M.; Adams, W. E., and Hrdina, L. S.: Bronchogenic Contamination in Embolic Abscess of the Lung, p. 1262 of this issue.

2. Cutler, E. C., and Schluter, S. A.: *Ann. Surg.* **84**:256, 1926.

3. Myerson, M. C.: *Laryngoscope* **32**:929, 1922. Hedblom, C. A.; Joannides, M., and Rosenthal, S.: *Ann. Surg.* **88**:823, 1928. Allen, D. S.: Etiology of Abscess of the Lung: Experimental and Clinical Studies, *Arch. Surg.* **16**:179 (Jan.) 1928.

4. Christie, R. V.; Ehrich, W., and Binger, C. A. L.: *J. Exper. Med.* **47**:741, 1928.

since the work of Meltzer and his associates,⁵ that inoculation of the bronchi with various types of pyogenic organisms frequently produces pneumonia. In man, also, aspiration pneumonia is a definite clinical entity. In pneumonia, the parenchyma of the lung is invaded by bacteria and heavily infiltrated by polymorphonuclear leukocytes to the extent that the cut surface of a specimen drips with pus, and yet the tissue vitality is regularly maintained; if the individual survives, resolution takes place speedily and without persisting cellular alterations. Another tissue thus heavily infected regularly breaks down and develops abscess. This difference between the lung and other tissues must be explained by assuming for the lung a much greater vitality in the presence of infection.

It may well be that this greater vitality is related to the matter of blood supply, for the lung receives a much greater volume of blood in proportion than does any other organ or tissue. In addition to the supply from the bronchial arteries, which is comparable to that alone *enjoyed by most other tissues, the lung receives through its capillaries* from the pulmonary artery the entire mass of circulating blood at each cycle. But to say that reduction of this blood supply by embolic occlusion of the pulmonary artery devitalizes the tissues lacks demonstration. Karsner and Ash⁶ and Krampf⁷ showed that bland embolism produces relative ischemia of the sector of lung involved and that this persists but does not produce tissue alterations. The bronchial circulation is sufficient to maintain the life of the parenchyma, and only when additional vascular injury is instituted, do changes occur interpretable as phenomena of devitalization.

The object of the experiments to be presented is to test the validity of the following hypothesis:

The greater vitality of the lung in infections is due mainly to a greater blood supply, and elimination of the pulmonary circulation reduces the blood supply and tissue vitality to the common level.

For this purpose, the reaction of the normal lung to intrabronchial contamination is compared to that of the lung which is the seat of bland embolism and is, therefore, nourished only by the bronchial circulation.

EXPERIMENTAL WORK

The experiments were divided into three groups. Dogs were used throughout.

The purpose of the first group was to determine the effect of a sterile embolus of small size on the parenchyma of the lung; that of the second to determine the results of intrabronchial insufflation of infectious material; and that of the third the reaction of the lung to a combination of bland embolism and septic insufflation.

5. Wollstein, Martha; and Meltzer, S. J.: J. Exper. Med. **16**:126, 1912.
Lamar, R. V., and Meltzer, S. J.: J. Exper. Med. **15**:133, 1912.

6. Karsner, H. T., and Ash, J. E.: J. M. Research **27**:205, 1912.

7. Krampf, F.: Deutsche Ztschr. f. Chir. **189**:216, 1924.

The embolus used was a small, lead bird-shot. This could be localized in the tissues by roentgen examination. The embolus was introduced into the external jugular vein through a small incision. The inoculum for intrabronchial insufflation was sputum obtained freshly from patients with chronic suppurative pulmonary diseases. The sputum was thinned with saline to reduce its viscosity, and 0.3 cc. per kilogram of body weight was injected bronchoscopically into the right lower bronchus or, in the embolized dogs, into the bronchus which supplied the embolized lobe of the lung. Introduction of an embolus and septic insufflation were utilized at the same sitting in the third group of experiments.

Local anesthesia (procaine hydrochloride, 0.5 per cent) with morphine was used for operation in group 1, in order not to risk bronchial contamination which might take place by aspiration under general anesthesia. The other animals were anesthetized by subcutaneous injection of sodium barbital, 0.3 Gm. per kilogram of body weight, and morphine. This induced deep sleep and inhibition of the cough reflex for from eighteen to twenty-four hours.

The behavior of all dogs was carefully noted. When they died from disease or were killed within fourteen days, postmortem examination was made with special reference to the gross and histologic appearance of the lungs.

In presentation, the material will be grouped and illustrated by characteristic protocols in brief.

GROUP 1.—In this group the effect of a sterile embolus alone was determined on six dogs. Five of them were killed on the eighth day, apparently in normal physical condition. At autopsy, four presented no gross or histologic evidence of alteration in the parenchyma of the lung at the embolus or elsewhere. The fifth showed a single spot of hemorrhagic infiltration lying in the lung margin distal to the embolus. In another lobe was a patch of resolving pneumonia typical of distemper, and the bronchi were injected and contained mucus.

The sixth dog died on the seventh day with symptoms of acute respiratory infection. The lungs contained extensive areas of pneumonic consolidation. The bronchi were filled with pus. In the right upper lobe was a sharply demarcated pyramidal area of gangrene, with the embolus situated at its apex near the hilum. The pleural cavity held 200 cc. of bloody fluid.

GROUP 2.—In this group the effects of intrabronchial insufflation alone was determined on twenty-two dogs. For six dogs, sputum was used from a case of bronchiectatic abscess of the lung and contained *Fungus nocardia*, cocci and rods. For the remainder, sputum was employed from a patient with bronchiectasis and contained fusospirochetes of Vincent, with cocci and rods. The observations in the two series were similar.

Ten dogs died in from one to four days with symptoms of respiratory infection; at autopsy they showed purulent bronchitis, edema and congestion of the lungs and, in some instances, bronchopneumonia. Thus:

*Protocol (dog 7).—*After recovery from the anesthetic, the animal remained quiet and refused food. On the third day, it became weaker and began to cough. Mucopus dripped from the nostrils. Dyspnea developed the following day, and the dog died. Autopsy showed the pleural cavities about one third filled with purulent fluid. The bronchi contained frothy pus, and the lungs presented several patches of bronchopneumonic consolidation. These areas showed no softening or abscess formation. Histologically, the parenchyma was massively infiltrated with polymorphonuclear leukocytes, and the vitality of the tissues was preserved at all points.

The remaining twelve dogs survived and were killed twelve days after insufflation. Seven presented normal lungs, three had purulent bronchitis, and two multiple areas of bronchopneumonia. The consolidated parts were firm and infiltrated with pus, but without abscess formation or other sign of loss of tissue vitality.

Group 3.—In this group the effect of a sterile embolism plus intrabronchial insufflation was determined on thirty-six dogs.

For ten dogs, sputum was used from a case of bronchiectasis containing non-specific pyogenic cocci and rods. For the others, the sputum was the same as for the second series of group 2 and contained Vincent's fusospirochetes, cocci and rods.

The effects in both series were similar. Seven dogs died in two days with purulent bronchitis and pulmonary edema and congestion. Three of these showed no alteration whatsoever in the embolized part of the lung, and four presented hemorrhagic infarct-like areas. Thus:

Protocol (dog 12).—Death occurred on the second day, preceded by symptoms of acute respiratory disease. On examination, the bronchi were found injected and containing mucopus. The lungs were heavy and red but air-containing, and on section dripped thin bloody fluid. The embolus was situated at the center of the left lower lobe in the lumen of an arteriole, and the lung substance peripheral to this point, in a pyramidal area, was infiltrated with blood and firmer in consistency than the surrounding lung, although air-containing. Figure 1 gives the microscopic appearance of this tissue. The alveolar septums are seen to be packed with extravasated red blood corpuscles.

Four dogs died in from four to seven days with purulent bronchitis, bronchopneumonia and hemorrhagic infarction of the lung. The pneumonic areas were similar to those in group 2 (dog 7), and the infarcts the same as that in dog 12 of this group.

Twenty-five dogs survived and were killed on the twelfth day. These may be classified according to the type of lesion presented, as follows:

Thirteen had purulent bronchitis of various degrees of severity, and the embolized parts of the lungs presented hemorrhagic infarct formation. These infarcts differed little from that of dog 12.

Four showed bronchitis, bronchopneumonia and hemorrhagic infarct.

Five had bronchopneumonia, and the embolized zone presented atelectasis. Thus:

Protocol (dog 32).—During the first seven days after inoculation, the animal appeared sick, refused food and lost weight markedly. There were no respiratory symptoms. At autopsy on the twelfth day, the bronchi were found to hold a moderate amount of mucopus and the parenchyma to have firm, elevated, airless gray patches, infiltrated with pus but intact and without abscess formation. The embolus was found in the center of the right middle lobe, and the surface of the lung distal to this was depressed, smooth, dark gray and airless. Section showed this solid tissue to extend into the parenchyma from 2 to 3 mm. from the surface only, and the tissues beneath were more fibrous than normal, but air-containing. No evidence of active inflammation was present. On blowing into the bronchus of the lobe to inflate the lung, the solid area did not fill with air. This lesion is illustrated in figure 2 in specimens from three of the dogs.

Two showed bronchitis, bronchopneumonia and septic infarction. Thus:

Protocol (dog 17).—Depression, anorexia, increasing weakness, and finally cough and nasal discharge followed the inoculation. Extreme dyspnea preceded death in twelve days. At autopsy, the lungs showed multiple areas of consolida-

tion, swollen, gray and exuding pus on section. The histologic appearance of these areas was that typical of bronchopneumonia, as in dog 7, and without loss of tissue vitality (fig. 3). The embolus was lodged in the left upper lobe near the hilum (fig. 4). Distal to this point was a sharply demarcated area of infarct distribution that was consolidated but presented a different appearance from that of the consolidated patches elsewhere. The surface was covered with fibrin and adherent to the parietal pleura. At several points the surface was ulcerated and, on being detached from the wall of the chest, exuded pus. The consistency of the underlying lung was soft. On section, it was uniformly gray and the tissue

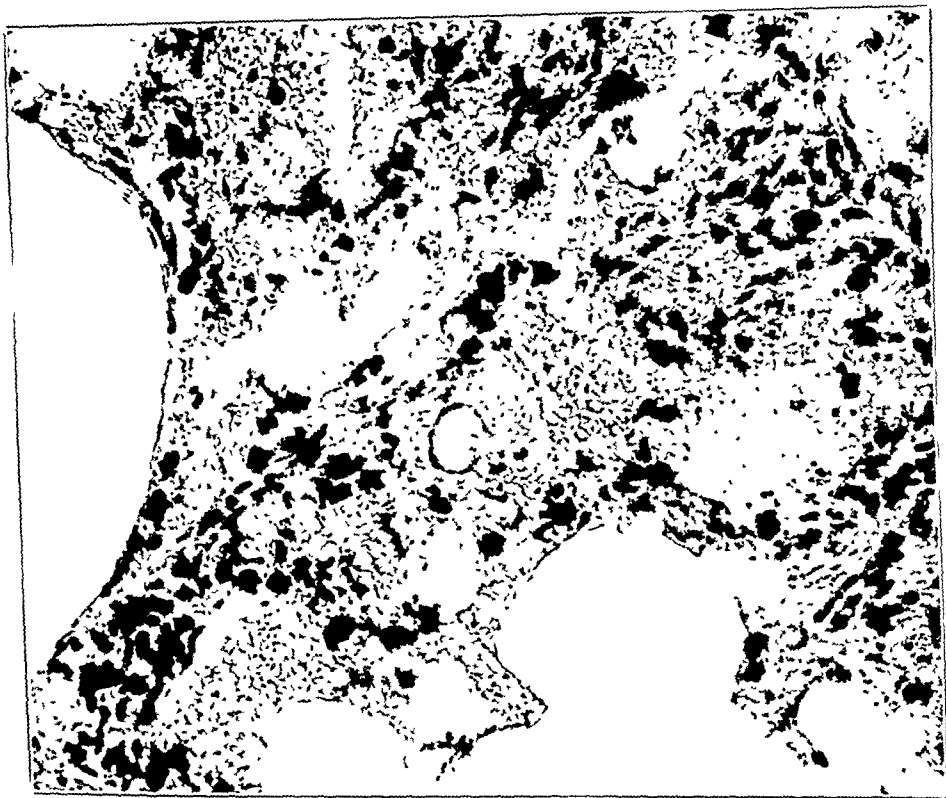


Fig. 1 (dog 12).—Photomicrograph of the infarcted area of the lung two days after bland embolism and septic intrabronchial insufflation. Note the extravasation of the red blood corpuscles in the alveolar walls.

at points liquefied and degenerated into abscesses containing thick pus and debris. At other parts, and particularly in the region of the interlobular septums, the parenchyma appeared viable although heavily infiltrated with purulent exudate. Histologically, the lung in this sector was found largely gangrenous and infiltrated with polymorphonuclear leukocytes (fig. 5). The bronchioles and the connective tissues immediately surrounding them were intact, but also infiltrated.

A similar picture of septic infarction with focal necrosis was shown by the other dog and is illustrated in figure 6.

Dog 14 presented purulent bronchitis, bronchopneumonia and abscess

Protocol (dog 14).—The dog was acutely ill after insufflation and until it was killed in twelve days. The trachea and bronchi contained considerable mucus. While there was a general pulmonary congestion, the only significant lesion found was in the left upper lobe (fig. 7). The distal surface of the lobe was firmly attached to the parietal pleura and the distal half of the lobe was occupied by a single abscess cavity filled with foul smelling pus. Immediately adjacent to the abscess on its proximal side and embedded in a vessel lumen in relatively normal parenchyma of the lung was found the embolus.

Dog 25 had bronchitis, bronchopneumonia and gangrenous infarction

Protocol (dog 25).—When killed on the twelfth day, the dog was severely ill and had been progressively so for many days, with cough, loss of appetite and failing weight and strength. Autopsy showed the lungs partly collapsed by an

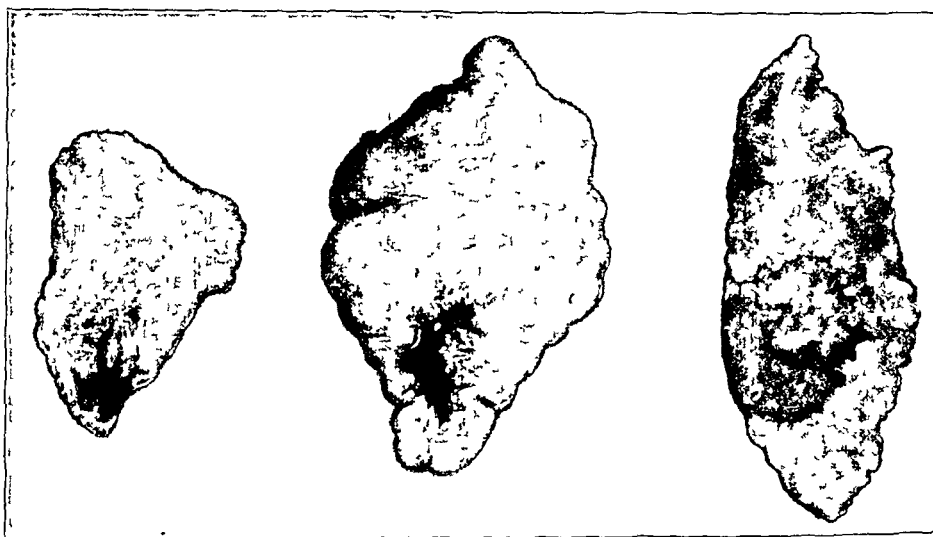


Fig. 2.—Lobes of three dogs twelve days after bland embolism and septic intra-bronchial insufflation. The embolized sector presents a patch of superficial chronic atelectasis.

accumulation of thin, purulent, foul fluid in the pleural cavities. There was an intense purulent bronchitis and general pulmonary congestion and edema. The left upper lobe (fig. 8) was attached to the parietal pleura with fibrin strands that separated easily. The lobe was sharply divided into two nearly equal parts, one air-containing and similar in appearance to the other lobes, and the other airless, soft and black. On section, the latter portion was uniformly black, soft and friable, and the embolus was found just proximal to it. Microscopically, the infarcted tissue was totally and uniformly necrotic.

Summary of Results.—Sixty-four dogs comprised three groups of experiments. In six dogs, sterile embolus was given alone. One died of pneumonia on the seventh day and showed a gangrenous infarct of

the lung. The remaining dogs were killed on the eighth day. One had a small area of hemorrhagic infiltration in the embolized zone and a bronchopneumonic infiltration elsewhere. The other four were free from pulmonary infection and showed absolutely no change in the embolized portion of lung.

Twenty-two dogs were inoculated intrabronchially with sputum from patients with chronic suppurative diseases of the lungs. Ten of these died within four days from toxemia and showed bronchitis, pulmonary congestion and pneumonia. Twelve survived, and on the twelfth day two showed bronchopneumonia, three purulent bronchitis, and seven had normal lungs. In none of this group was there pulmonary abscess

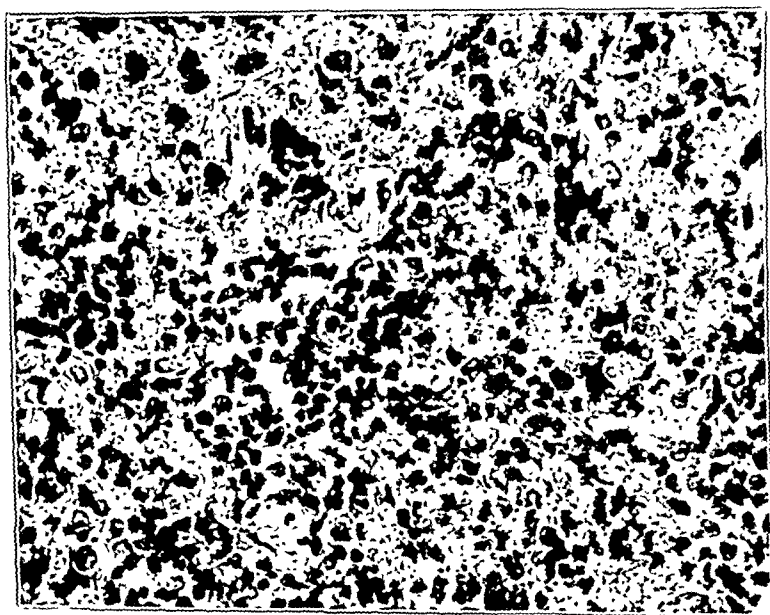


Fig. 3 (dog 17).—Photomicrograph of the lung with insufflation pneumonia at twelve days. Note the retention of tissue vitality.

formation or other evidence of devitalization of the parenchyma of the lung.

Thirty-six dogs received both sterile embolus and intrabronchial sputum inoculation. Seven died in two days from toxemia and showed bronchitis and pulmonary congestion. The embolized portion of the lung was hemorrhagic in four and unchanged in three. Four other dogs died in from four to seven days, with bronchitis, bronchopneumonia and hemorrhagic infarction. The remaining twenty-five survived until killed in twelve days; autopsy showed a variety of lesions in the embolized segment of the lung. Thus, seventeen dogs had hemorrhagic infarcts, five atelectasis of a chronic type, two inflammatory consolidation with

focal necrosis, one solitary abscess formation, and one frank massive gangrene.

COMMENT AND CONCLUSIONS

These experiments demonstrate different effects following intra-bronchial inoculation of lung that has been embolized from those which occur after such inoculation of normal lung or from the embolus acting alone.

Where bland embolism was employed alone, no cellular alterations appeared in the segment of lung affected, in four of six dogs so treated. It is significant that in the remaining two animals, where changes did occur, viz., hemorrhagic infarction and gangrenous infarction, other

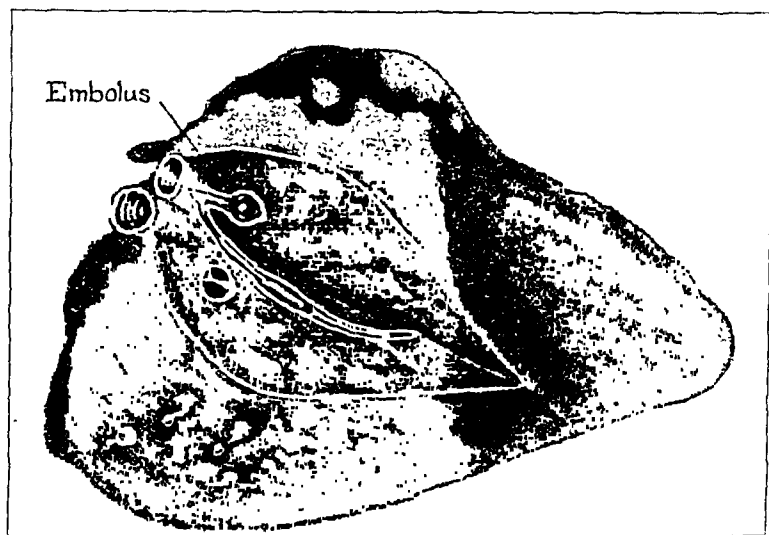


Fig. 4 (dog 17).—Left upper lobe twelve days after bland embolism and septic intrabronchial insufflation. The infarcted zone presents foci of necrosis, some of which extend to the pleural surface.

parts of the lungs displayed evidences of infection acquired spontaneously. The infarct lesions were similar to those appearing in group 3 in which the lung was intentionally infected. Accordingly, this group alone suggests that bland embolism affects no cellular alterations unless the lung is infected.

Intrabronchial inoculation of the normal lung resulted in a high mortality from toxemia and pneumonia. Several animals, on the other hand, were not made appreciably ill and in twelve days showed no lesions other than bronchitis. Others developed pneumonia and were recovering when killed. In none of these twenty-two dogs was there devitalization of the lung and abscess formation, although every opportunity was

afforded for inducing suppuration by using highly virulent and specific bacteria (Vincent's fusospirochetes and *Fungus nocardia*) in mixtures with other pyogenic organisms from a focus of pulmonary suppuration and by depressing cough reflexes and retaining the inoculum in contact with the lung for many hours after inoculation.

Intrabronchial inoculation combined with bland embolism resulted in hemorrhagic infarction in twenty-five of the thirty-six dogs so treated. Five showed chronic atelectasis, two inflammatory consolidation with focal necrosis, one solitary abscess, and one massive gangrene. Striking features in these lesions were that the embolus lay just proximal to the

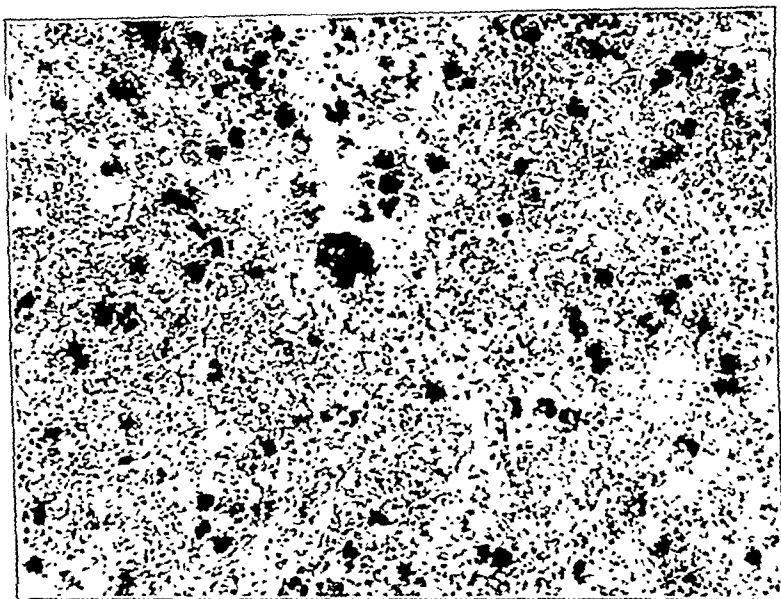


Fig. 5 (dog 17).—Photomicrograph of the embolized sector of the lung twelve days after bland embolism and septic intrabronchial insufflation. Note the loss of tissue vitality.

lesion and embedded in normal lung, and that the lesion was strictly confined to the territory supplied by the embolized vessel. Elsewhere, in nonembolized parts of the lung, the same effects of the bronchial contamination appeared as in animals not receiving embolus (group 2).

The various alterations which thus appeared in response to a combination of intrabronchial inoculation with sterile embolus are interpretable on a basis of alterations in tissue vitality. Thus, the extreme change, i. e., massive gangrene, represented total and uniform tissue death; solitary abscess formation represented central devitalization plus infection; septic infarct formation showed devitalization of parts only

that were farthest from the bronchial vessels, plus infection; atelectasis was the result of bronchial obstruction from fibrosis of foci of necrosis; and hemorrhagic infarction of the otherwise intact parenchyma of the lung must have occurred from fragility and rupture of the capillary wall.

One factor in these animals to account for this reduction of vitality is embolic obstruction of the pulmonary blood supply, but in group 1 it is shown that such does not occur from embolus alone. Another prominent circumstance is contamination of the bronchial tree with infectious material; but the essential factor here is probably not the direct necrotizing action of the bacteria, for tissue vitality was lost first by the parts farthest from the bronchi, and in the least grade of lesion, hemorrhagic infarction, there was no evidence of infection of the

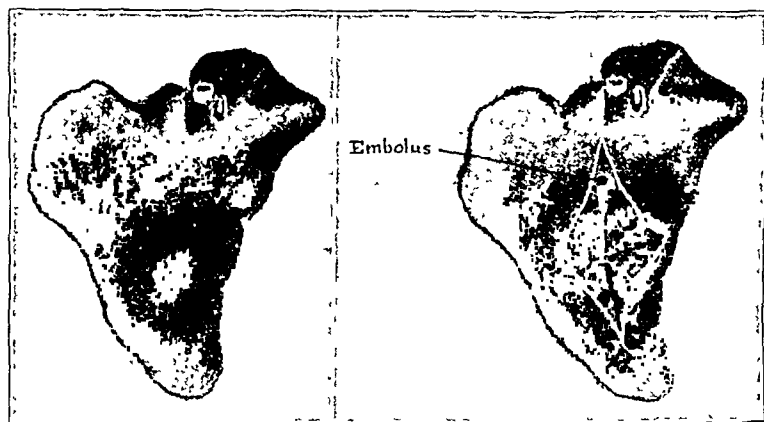


Fig. 6 (dog 18).—Right lower lobe twelve days after bland embolism and septic intrabronchial insufflation. The infarcted area presents foci of necrosis.

parenchyma. Additional vascular occlusion was evidently the factor supplied by the intrabronchial contamination. Thus, bronchitis produced peribronchial congestion, and this jeopardized the blood supply of parts at a distance to the bronchi which after pulmonary embolism rely practically entirely on the bronchial vessels. Of course in addition to vascular occlusion from these two sources, devitalization was contributed to by direct bacterial action to a considerable degree in the severer lesions.

It may be concluded, accordingly, that lung tissue which retains only its bronchial blood supply behaves toward pyogenic infection in a manner similar to that of other tissues having a blood supply of corresponding amount; that is, where the infection is sufficiently virulent focal or diffuse necrosis occurs.

It should be pointed out that the suppurative process produced in the lung by combining bland embolism with bronchial contamination is of a different nature from that which results from a septic embolus. In the former it is diffuse and occupies more or less uniformly the entire embolized sector of lung, since the infection arises in all parts from the bronchial tree, while in the latter it centers at the embolus and lacks infarct distribution.

The principle of ischemia in infections of the lung probably has clinical significance. Thus, it may pertain to postoperative pulmonary complications, since both embolism and bronchial contamination occur

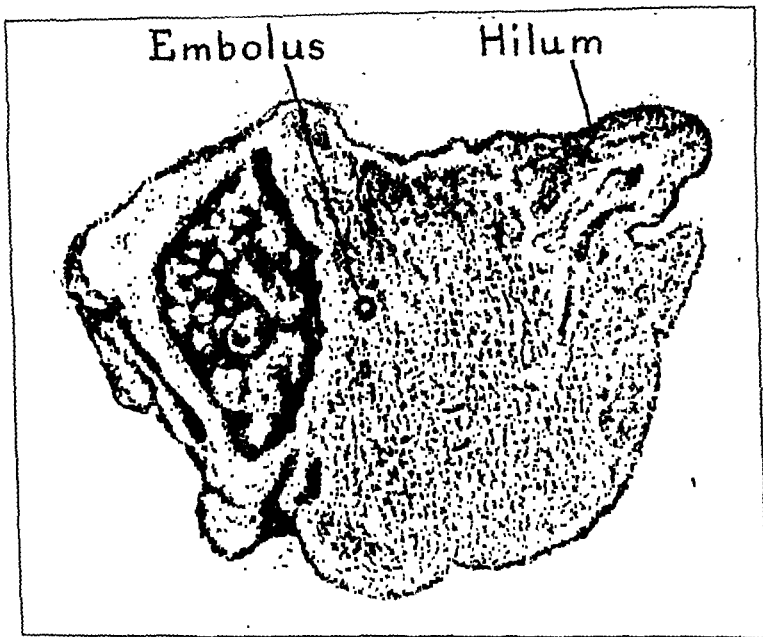


Fig. 7 (dog 14).—Left upper lobe twelve days after bland embolism and septic intrabronchial insufflation. The cut surface of the lobe is seen and presents a large abscess lying distal to the embolus.

in conjunction with surgical operations.¹ If, in the presence of intrabronchial infection, a small fragment of blood clot from near the operative field lodges in the lung, what might otherwise have been an uncomplicated bronchitis or pneumonia may develop into a suppurative lesion. This could occur whether the embolus were sterile or infected and may account for certain pulmonary abscesses following sterile operations.

Thrombosis of a pulmonary arteriole would have the same effect as embolism, and this suggests an explanation for certain other phenomena of suppurative diseases of the lung. Postpneumonic abscess of the lung

may be caused by thrombosis of an arteriole lying within the pneumonic area; indeed, the rarity of arterial thrombosis in pneumonia, as far as we are acquainted with it, makes this the more plausible, since abscess after pneumonia is also rare. Likewise relapses and abrupt changes for the worse that are occasionally seen in pulmonary suppuration, with new extensions of ulceration and gangrene, are probably the result of thrombosis and devitalization of new parts. Empyema complicating pneumonia, especially where cortical "abscesses" are seen and where bronchopleural fistula appears, may be caused by thrombosis of a peripheral cortical vessel.

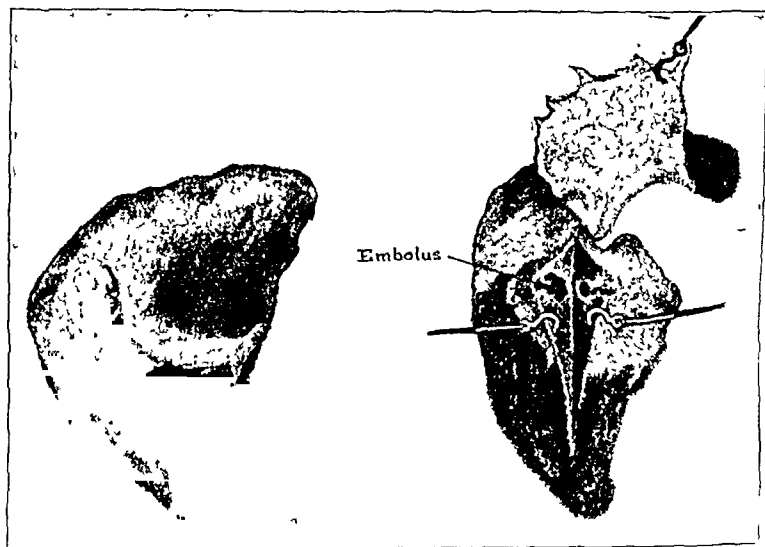


Fig 8 (dog 25) —Left upper lobe twelve days after bland embolism and septic intrabronchial insufflation. The distal half of the lobe is gangrenous.

It should be emphasized that obstruction of the pulmonary artery in the presence of bronchial contamination does not necessarily lead to softening and suppuration, for this occurred in only four of thirty-six dogs. Also, there is no appreciable tendency for localization of infection in the embolized area; indeed, in these dogs pneumonia often existed only in nonembolized parts. Evidently, the bronchi of an embolized zone, since they retain their normal blood supply are no less susceptible to infection and serve to protect the surrounding parenchyma from it in a normal fashion; but once the infection succeeds in invading the parenchyma, it finds ready medium in the devitalized parenchyma.

SUMMARY

Attention was called to the facts that abscess develops much more readily from embolic than from intrabronchial inoculation of the lung, and that the lung appears to be in general much more resistant to necrosis and suppuration than are other tissues.

Experimental test was made of the hypothesis: The greater vitality of the lung in pyogenic infections is due mainly to a greater blood supply, and elimination of the pulmonary circulation, as by embolism, reduces the blood supply and tissue vitality to the common level.

It was concluded that the hypothesis is essentially correct. This principle was applied to explain the pathogenesis of certain suppurative diseases of the lungs, viz., postoperative abscess of the lung especially following sterile operations, postpneumonic abscess of the lung and empyema, and relapses in suppurative diseases of the lung in general. Hemorrhagic infarct may have a similar origin.

PULMONARY ABSCESS

AN ANALYSIS OF ONE HUNDRED AND SEVENTY-TWO CASES*

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PHILADELPHIA

Suppurative lesions in the lungs result from pyogenic organisms entering by way of the air passages and the blood stream, or by direct extension from contiguous structures. The term pulmonary suppuration has been used rather indiscriminately to include both abscess and bronchiectasis and while these lesions may be associated, an effort should be made to differentiate them clinically. The term pulmonary abscess as used here refers to the circumscribed suppuration which eventuates in cavity formation, softened tuberculous areas and bronchiectasis being excluded. Among 172 cases which constitute the basis of this report, no abscess due to the aspiration of a demonstrable foreign body or secondary to new growth has been included. These types of pulmonary abscess have certain distinctive pathologic and clinical features which call for separate consideration. Reference will be made to them when the diagnosis is considered.

Among the 172 cases in our group, 108 occurred in males (62.8 per cent) and sixty-four in females (37.2 per cent). The age of the patients varied from 1½ to 66 years, the average being 31 years. The percentage of distribution of the cases by decades is as follows: first decade, 6.4 per cent; second decade, 10.5 per cent; third decade, 27.9 per cent; fourth decade, 30.8 per cent; fifth decade, 18.6 per cent; sixth decade, 3.6 per cent and seventh decade, 2.3 per cent. While pulmonary abscess may occur at any age, one half of the cases in our series occurred in patients between 20 and 40 years. This is in contrast to the predominance in the earlier years of life of the pulmonary suppuration due to aspirated foreign body, and the increasing frequency in later years of pulmonary abscess associated with new growth.

ETIOLOGY

Etiologically, the cases in this series fall in three main groups:

Pulmonary Abscess Following Surgical Operation.—This group includes 121 of the 172 cases, or approximately 70 per cent of the

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series. The operations were: (a) tonsillectomy, ninety-seven instances (general anesthesia in eighty-eight, local anesthesia in four, anesthesia not stated in five); (b) oral operations, such as tooth extraction, etc., ten instances (general anesthesia in seven, local anesthesia in three); (c) operations in other parts of the body, e.g., appendectomy, herniorrhaphy, etc., fourteen (general anesthesia in eight, anesthesia not stated in six). Tonsillectomy constituted 56 per cent and tonsillectomy and oral operations 62 per cent of all the cases.

Pulmonary Abscess Following Acute Infection of Respiratory Tract.—This group includes forty-three of the 172 cases, or approximately 25 per cent of the series. Difficulty was encountered in determining the character of the respiratory disease preceding the onset of the pulmonary abscess. According to the patient's history, an acute infection of the respiratory tract, variously called "an acute cold," influenza, acute bronchitis, preceded the symptoms of abscess in twenty-two instances, or approximately 13 per cent of the whole series. Pneumonia was stated to precede the occurrence of abscess in sixteen instances or 9.3 per cent of the series. In five of these cases there was a complicating pleurisy, and in one a rib resection had been done for empyema. In two cases each, a simple acute pleurisy without effusion and bronchopneumonia were stated to have preceded the onset of pulmonary abscess.

It is our opinion that the acute respiratory lesions considered as antecedent to the occurrence of abscess of the lung probably represent variations in the severity of the initial manifestations of the pyogenic infection. Occasionally, with widespread pyogenic infection, the acute onset and diffuse character of the pulmonary lesion grossly resemble lobar pneumonia. Later, with localization and distinct abscess formation, the sequence of events may easily be misinterpreted as abscess complicating or following lobar pneumonia.

Miscellaneous Group.—In this group the abscess was said to follow a chest injury (automobile accidents, stab wound with empyema) in two instances, drowning accidents in two instances, poisoning from sewer gas in one instance, and from unknown causes in three instances.

The infection in pulmonary abscess is usually polymicrobial. Our associate, C. J. Bucher, has in preparation the complete report of the bacteriologic observations in our patients. His studies have been made on specimens collected by direct bronchoscopic aspiration or at operation. Spirochetes and fusiform bacilli are commonly found in association with pyogenic cocci.

SITE OF THE ABSCESS

While pulmonary abscess may be single or multiple and occur in any part of the lung, they were found to be localized in one lobe in

79.3 per cent, in two lobes in 19.5 per cent, and in three lobes in 1.2 per cent of the 169 cases of our series in which accurate localization was attempted by combined physical, roentgenologic and bronchoscopic examinations. It is often stated that the lower lobes, and especially the right, are more frequently involved. In our experience, involvement of the upper lobe is more common.

CLINICAL MANIFESTATIONS

F. T. Lord has pointed out that the symptomatology of the post-operative and nonoperative group does not vary materially. This has been our experience. One of us (Clerf¹) analyzed carefully the time of onset and the development of the symptoms after tonsillectomy in forty-seven cases. The time of onset of symptoms varied from one to thirty-five days. The average time of occurrence of definite symptoms (pain, fever, chills or chilliness, cough with or without expectoration,

TABLE 1.—*Distribution of Pulmonary Abscesses*

Monolobar Lesions (131 cases)	
Right upper lobe.....	49
Right middle lobe.....	10
Right lower lobe.....	22
Left upper lobe.....	30
Left lower lobe.....	23
Multilobar Lesions (35 cases)	
Unilateral (33 cases)	
Right middle and lower lobes.....	14
Right upper and lower lobes.....	4
Right upper and middle lobes.....	4
Left upper and lower lobes.....	11
Bilateral (2 cases)	
Right middle and lower lobes and left upper lobe.....	1
Right upper and middle lobes and left upper lobe.....	1

and hemoptysis) was seven and two-tenths days. Often the patient was listless and irritable for several days before the onset of distinct symptoms. A brief period of malaise with general weakness and slight fever is not uncommon after uncomplicated tonsillectomy. Not infrequently it is stated that the patient "caught a cold" while at the hospital or more often, when returning home.

Pain referred to some part of the chest was the most commonly observed early symptom. It is described as sharp, stitchlike, or stabbing, made worse by coughing or deep breathing, and suggests the pain of pleurisy. In one case, it came on twenty-four hours after operation. In twenty-two cases (46 per cent), pain was the first symptom and was observed within four days following operation.

Fever, without chill or chilliness, occurred as the first symptom in eight cases (17 per cent). It is present at some time or other in practically all cases, and usually subsides after adequate drainage has been

1. Clerf, L. H.: Lung Abscess Following Tonsillectomy, *Atlantic M. J.* **31**: 911 (Sept.) 1928.

established. Continuance of fever after drainage has spontaneously occurred suggests either an extension of the infective process or defective drainage. A recrudescence in the later stages of the disease usually indicates interference with drainage. Fever with chills or chilliness was noted as the first symptom in six cases (13 per cent). Severe rigors, uncommonly observed, usually indicate extension of the pulmonary lesion.

Cough, without expectoration, was the first complaint in eleven cases (23 per cent). With rupture of the abscess into a bronchus, cough becomes a frequent and distressing symptom and is associated with expectoration of purulent material. The earliest occurrence of purulent expectoration was five days after operation, a large quantity of fetid pus being evacuated. The longest interval was forty-eight days after operation. In twelve cases (25 per cent) purulent expectoration was observed on or before the seventh day.

The material first expectorated varied in quantity and in appearance. In several cases a large quantity (from 1 to 2 cupfuls) of dark fetid material suggesting decomposed blood was expectorated within several hours.

Hemoptysis as a first symptom did not occur in any of the cases in this special group. In one instance a considerable quantity of blood was expectorated on the seventh day.

The onset and development of symptoms (the clinical picture) are more important in the diagnosis in the individual patient than the total of the symptoms occurring in the individual or in the group. The following tabulation prepared from the history taken on admission in 114 cases gives some idea of the relative frequency of the symptoms: cough, 99.1 per cent; expectoration, 86.8 per cent; pain, 71.5 per cent; hemorrhage, 44.7 per cent; dyspnea, 13.1 per cent, and fever, with or without chilliness or chills, 62.2 per cent.

The blood count revealed a great variation in the number of leukocytes, a count within the normal range being not uncommon. A moderate secondary anemia was common; a pronounced anemia occurred in about 20 per cent of the cases.

DIAGNOSIS

The determination of the presence and the location of a pulmonary abscess requires a consideration of the history, symptoms and signs, studies of the sputum, roentgenologic observations and bronchoscopy. The occurrence of cough and fever after operation, especially about the upper respiratory tract, should focus attention on the possibility of pulmonary abscess. The sudden appearance of purulent expectoration, or the occurrence of a severe paroxysm of cough during which considerable pus is expectorated, is highly significant, although this may

occur in perforating empyema and perforating subdiaphragmatic abscess. The presence of elastic fibers in the sputum in the absence of tubercle bacilli is evidence of a nontuberculous destructive lesion. The physical signs are not distinctive. The small deep-seated abscess may give rise to marked symptoms and indefinite signs. In the larger and more superficial abscesses the signs are usually those of consolidation which may occur in any part of the chest. A pleuritic friction sound is common, though frequently overlooked. Distinct cavity signs are so infrequent in pulmonary abscess that their absence should have no weight in diagnosis. The roentgen and bronchoscopic examinations are invaluable in the complete diagnostic study and aid particularly in the localization of the lesion. Such localization is essential in the consideration of therapy.

The conditions to be differentiated from pulmonary abscess are:

1. Tuberculosis. Pulmonary abscess, especially of the upper lobes, may easily be mistaken for pulmonary tuberculosis unless the history, the character of the sputum, including the presence of tubercle bacilli, and the roentgenologic observations, are carefully considered. Patients with pulmonary abscess are not infrequently referred to tuberculosis sanatoriums.

2. Bronchiectasis. In recent cases of pulmonary abscess, the differentiation from bronchiectasis is usually not difficult. The history and the observations on physical, roentgenologic and bronchoscopic examinations are usually conclusive. In the cases of long standing, however, the lesions of abscess and bronchiectasis present so much in common and so frequently co-exist that the differentiation may be difficult (fig. 1A and B).

3. Pulmonary suppuration due to aspirated foreign body. This is more common during the early years of life, but may occur at any age. The history may be inconclusive and the latent interval between aspiration and the development of pulmonary symptoms may be misleading. The symptoms and signs may resemble those of nonforeign body abscess; however, in cases of foreign bodies the asthmatoïd wheeze, the tendency of the signs to change with the shifting of the foreign body and the occurrence of signs of bronchial obstruction are commonly found. The roentgenologic and bronchoscopic examinations are conclusive.

4. Interlobar empyema. The physical signs are most marked in the region of the interlobar septum; there may be some displacement of the heart, and the sputum, if purulent, rarely contains elastic fibers. The roentgenologic observations are important.

5. Neoplasm. Diagnostic bronchoscopy is the only method by which primary new growth in the lung or pulmonary abscess secondary to pri-

mary new growth can be recognized with certainty unless extrathoracic metastases are present.

6. Syphilis and the mycotic infections. These are rare. The history, concomitant evidence of syphilis or of the mycoses in other parts of the body, the Wassermann test, and the studies of the sputum are important.

7. Pulmonary gangrene. The distinction is not difficult in the typical case with marked fetor of the breath and sputum and profound systemic disturbance. In other instances the lesions of abscess and gangrene so closely resemble each other that differentiation is not possible. The finding of spirochetes and fusiform bacilli does not serve to differentiate the two conditions.

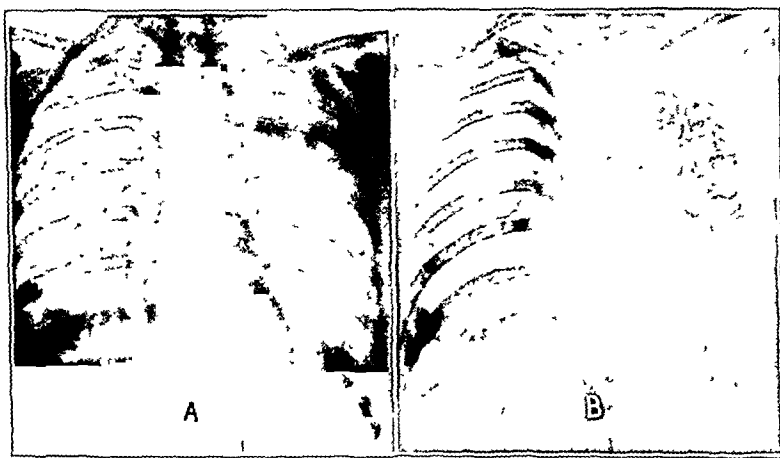


Fig. 1.—Post-tonsillectomic abscess involving the upper lobe of the left lung. *A*, a roentgenogram made after admission of the patient to Jefferson Hospital, shows a single abscess with multiple cavities. Bronchoscopic treatment was instituted with marked improvement in the acute symptoms; surgical intervention was delayed because of this improvement and later, when resorted to, was probably inadequate. *B* is a pneumonogram demonstrating development of bronchial dilatations throughout the left lung. Thoracoplasty is indicated for the bronchiectasis.

PROGNOSIS

F. T. Lord² stated that the expectation for life of patients with pulmonary abscess has never been accurately determined, and from an analysis of a large group of cases concluded that the theoretical outlook in unoperated pulmonary abscess may be estimated as a mortality of about 74 per cent. Lord estimated that under medical treatment alone recovery occurs in about 11 per cent, and incomplete recovery

2. Lord, F. T.: *Diseases of the Bronchi, Lungs and Pleura*, ed. 2, Philadelphia, Lea & Febiger, 1925, p. 460.

occurs in about 15 per cent of the cases. Among 172 patients under our observation since 1923, eleven are considered as untreated because they were either referred for diagnosis only, securing treatment elsewhere, or because they have so recently come under observation (1 case) that an analysis of the present status cannot be made. Among the remaining 161 patients treated medically, bronchoscopically or surgically, eighty-one recovered (50.3 per cent), forty-eight were improved (29.8 per cent), eight were unchanged (5 per cent), two had a recurrence after apparent recovery (1.2 per cent) and twenty-two died (13.7 per cent). The prognosis is unquestionably influenced by a number of factors:

1. The severity of the pyogenic infection. In the presence of a virulent infection and widespread purulent pneumonia, or when multilobar abscesses or complications are present, the prognosis is grave.

2. The age and previous condition of the patient. These factors are important, especially in the group in which surgical intervention is indicated.

TABLE 2—Age of Patient in Relation to End-Result

Age Period	Recovery	Improved *	Unchanged	Death	Recurrence	Totals
1-10	8	1	1	1	0	11
11-20	8	7	0	2	0	17
21-30	21	15	3	7	1	47
31-40	23	15	2	8	0	48
41-50	17	6	2	3	1	29
over-50	4	4	0	1	0	9
Totals	81	48	8	22	2	161

* By improved is meant marked relief from subjective symptoms, diminution in the abnormal physical and roentgen changes, and marked clearing of the process on bronchoscopic examination.

3. The location of the abscess. Centrally located abscesses are amenable to bronchoscopic treatment, while peripherally located abscesses usually require surgical intervention.

4. The occurrence of complications. Cerebral abscess, cerebral embolism, hemorrhage, suppurative pericarditis, acute diffuse pneumonitis and endocarditis are all complications which feature in the high mortality rate.

5. The duration of the disease before bronchoscopic and surgical treatment is instituted.

6. The care with which patients are selected for the bronchoscopist and the surgeon. Obviously the sine qua non to recovery is adequate drainage either through the air passages or by external incision.

ROENTGENOLOGY IN DIAGNOSIS AND LOCALIZATION

The roentgenographic appearance of pulmonary abscess varies, depending on the stage of the disease, the location, and the presence or absence of complications, notably changes in the pleura.

Before drainage occurs, the involved area appears as a homogeneous density with poorly defined margins. In this stage the appearance is that of consolidation, and when the process follows pneumonia it is considered as delayed resolution. Acute suppurative pneumonitis may be mistaken for pneumonia.

Softening of the tissues and evacuation of the pus through a bronchus gives the roentgen appearance of a cavity containing fluid and air surrounded by a zone of increased density. Change in body position alters the relation of the fluid level in the cavity. The relative sizes of the inflammatory zone and the cavity vary greatly.

The conditions to be differentiated roentgenologically from pulmonary abscess are:

1. Tuberculosis. In tuberculosis with cavity formation there is usually an antecedent history of tuberculosis, the cavity commonly is apical, and there is often evidence of tubercle formation in the opposite lung. Tuberculous cavities rarely contain fluid in great quantity, while fluid is usually demonstrable in pulmonary abscess. Multiple cavity formation is more often demonstrable in tuberculosis than it is in abscess.

2. Neoplasm. Abscess secondary to pulmonary new growth, especially neoplasm of the bronchus, gives rise to no characteristic roentgenogram unless pulmonary metastases are present.

3. Bronchiectasis. Bronchiectasis uncomplicated by extensive changes of the pulmonary tissues is readily distinguished roentgenologically from pulmonary abscess (fig. 2). In this type, cavity formation is not evident on the simple roentgenogram; the increased markings are usually diffuse and occur in the lower portion of the pulmonary fields as an increased haze. The instillation of iodized oil in these cases reveals saccular or cylindric dilatations of the bronchi. Dilatations of the bronchi occurring as a result of pulmonary suppuration of long standing are not readily differentiated from their cause because they are accompanied by marked tissue changes producing on the roentgenogram a dense shadow in which the outlines of the cavities are lost. Pneumonography after bronchoscopic aspiration is the only method which will indicate the exact anatomic change and reveal the cavities which are present (fig. 1).

4. Interlobar empyema. Interlobar empyema is often differentiated with difficulty from pulmonary abscess. Before rupture, the interlobar collection of fluid presents a similar picture to that of abscess before cavity formation. After rupture and drainage, it may roentgenographically simulate the cavity of abscess. The history of a preceding pneumonia with the occurrence of the changes in the vicinity of the fissures is of value.

The best localization from the surgical standpoint is by the roentgen method, using postero-anterior and lateral exposures. In abscess of the upper portion of the upper lobe, localization in the lateral view is not always satisfactory and dependence must be placed largely on the physical examination.

Fluoroscopic localization with the patient in the position in which the operation is to be performed is of value, and should be done in the presence of the surgeon. Localization in relation to ribs is preferable to skin localization.

Determination of the most superficial portion of the abscess is most important because at this point the surgeon finds pleural adhesions if they are present.

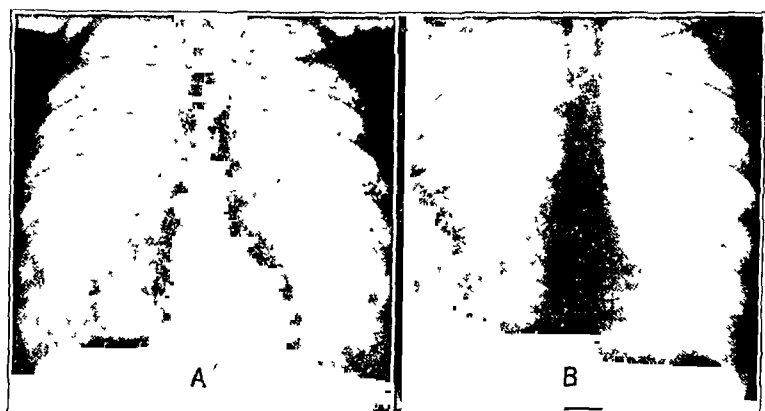


Fig 2—Bronchiectasis of the right lung of two years' duration complicated by the development of a pulmonary abscess *A*, a roentgenogram made before development of the abscess, shows extensive changes in the right lower lobe. *B* shows an abscess with fluid level which cleared up completely following external drainage. The wound healed Thoracoplasty is indicated for the bronchiectasis

In the typical abscess with cavity and fluid, the foregoing method is sufficient for localization. When the abscess is long standing and complicated by adjacent tissue changes and thickening of the pleura, bronchoscopic pneumonography is of value. Under fluoroscopic guidance it is possible to control the quantity to be instilled and to direct the bronchoscopist to the area of greatest involvement. Care must be taken that the pneumonogram does not mislead one; sometimes the oil collects in the parenchyma in a localized area in such a way as to simulate an abscess. Distinguishing features are that there is no fluid level and the iodized oil occupies an area free from disease on the roentgenograms made before the instillation.

The progress of the patient under treatment is readily determined by serial roentgenograms. The occurrence of complications such as new areas of involvement, metastatic abscesses or pleural changes may be recognized.

GENERAL CONSIDERATIONS OF TREATMENT

Medical treatment comprises rest, symptomatic care, attention to the diet and measures to improve the general condition of the patient. Medical treatment alone is indicated in the early acute phase of pyogenic infections before abscess formation has occurred. In other instances it is combined with bronchoscopic or surgical treatment or both. Caution is necessary in the administration of cough sedatives which favor stagnation, a factor in prolonging suppuration to a chronic or fatal issue. Postural drainage is important in supplementing bronchoscopic drainage in pulmonary abscesses located near the hilum and in communication with the tracheobronchial tree. In this location the abscess tends to drain spontaneously into the large bronchi but is frequently prevented from so doing by ciliary denudation, obstructing granulations or the weight and bulk of retained secretions. Bronchoscopic drainage is particularly indicated in this type of case. When the abscess is peripherally located in connection with only small terminal bronchi, drainage can rarely be established apart from external operation.

Our general attitude is to treat patients with pulmonary abscess conservatively, including bronchoscopy, unless surgical intervention is definitely indicated at the time the patient comes under observation. The possible advantage of surgical measures is considered in every patient, but they may be spared the external operation by careful bronchoscopic treatment. Conservative measures may prepare the patient for surgical intervention, but on the other hand, the disease should not be allowed to go on indefinitely until fibrosis and bronchiectasis occur and render the ultimate surgical intervention difficult and unsatisfactory. The whole problem of the treatment in the individual case requires close cooperation of the internist, roentgenologist, bronchoscopist and surgeon.

Artificial pneumothorax, in our opinion, is not only unsatisfactory but dangerous. Since the principal object of therapy in pulmonary abscess is to secure adequate drainage, it is difficult to understand the rationale of treatment by induced pneumothorax. In tuberculosis, rest and immobilization of the lung are primary considerations, while in abscess, drainage is the *sine qua non* to recovery. Whittemore and Balboni³ reported that among eighteen patients treated by this method,

3. Whittemore, W., and Balboni, G. M.: Nontuberculous Bronchopulmonary Suppurative Lesions: Results of Treatment by Artificial Pneumothorax, *Arch. Surg.* 16:228 (Jan.) 1928.

two were completely cured, two were temporarily improved, three died from hemorrhage from the lung during treatment, five developed empyema, of which one died. These observers conclude that the value of artificial pneumothorax in the treatment for pulmonary abscess is questionable.

Small transfusions of whole blood are of value in patients with marked secondary anemia, especially in the preparation for operation and in the after-care of those treated surgically.

BRONCHOSCOPY IN DIAGNOSIS AND IN TREATMENT

The ability of the bronchoscopist to inspect the interior of the larger bronchi and the orifice of the bronchial subdivisions renders bronchoscopy a valuable aid in diagnosis. Pus observed coming from the orifice of a bronchial subdivision is positive evidence of the presence of suppuration; whether the process is abscess of the lung, bronchiectasis or purulent bronchitis must be determined in conjunction with other methods of diagnosis.

The importance of a diagnostic bronchoscopy in all cases of pulmonary abscess, unless distinctly contraindicated, irrespective of the method of treatment to be employed has been repeatedly demonstrated. Abscess of the lung may be secondary to a neoplasm of the bronchus or an overlooked nonopaque foreign body. In either of these conditions, external drainage would be of questionable value. Bronchoscopy can positively establish the presence of bronchial obstruction and in the case of new growth a specimen of tissue can be removed for histologic examination. If the lesion is benign, it can often be removed bronchoscopically; if a foreign body is present, its removal will achieve cure in practically every case.

The accurate localization of a suppurative process occasionally presents difficulties. Often one cannot determine if the lesion is in the lower portion of the upper lobe or in the upper portion of the lower lobe. The bronchoscopist can definitely ascertain whether pus comes from one or the other bronchus, and in this way he can localize the suppuration with relation to the lobes of the lung and not infrequently to the subdivisions of one of the bronchi. In certain cases of pulmonary abscess it may become necessary to resort to pneumonography for the accurate localization of the cavity. Instillation of iodized oil into the cavity is often extremely difficult since the communication between the abscess and the draining bronchus is often tortuous and filled with secretion, granulation tissue and swollen and edematous mucosa. Methods of instillation which are dependent on gravity are rarely successful in these cases. The best results are obtained by the bronchoscopic method of instillation of the iodized oil performed on the fluoroscopic table so that the aid of the fluoroscopist may be secured

in determining the quantity of material to be instilled, also to ascertain if a certain bronchial subdivision actually communicates with the abscess cavity.

Bronchoscopic aspiration, in trained hands, can be safely and quickly carried out, and, in properly selected cases of pulmonary abscess it is one of the most efficient methods of treatment at our command. The excellent results obtained by a large number of bronchoscopists justify the opinion that bronchoscopy should be one of the methods of treatment to be considered in every case of pulmonary abscess.

Adequate drainage, which is the most important factor in the spontaneous recovery of these patients, can often be secured by bronchoscopy. This is accomplished by the removal of obstructing masses of granulation tissue, by the aspiration of the large quantity of pus which overtaxes ciliary activity (Jackson) in the smaller bronchi and by the removal of secretions from the abscess cavity with the aid of small, flexible-tipped, aspirating tubes.

Every case of abscess is not suitable for bronchoscopic aspiration; this must be determined by careful study of the patient by the internist, the roentgenologist and the surgeon. The matter of teamwork in determining the proper method of treatment and in following the subsequent progress of the patient has been discussed elsewhere. Its importance cannot be overemphasized (fig. 3).

Duration of the disease need not necessarily be a determining factor in deciding on bronchoscopy; in recent cases of abscess there is invariably more favorable response than in those of prolonged duration. In the latter cases, however, remarkable results have been obtained following a course of bronchoscopic aspiration.

In our series, 127 patients with abscess of the lung were referred for bronchoscopic treatment. This group does not include those cases in which surgical intervention was indicated when the patients first came under our observation, cases in which a diagnostic bronchoscopy was done preliminary to external drainage or cases of abscess of the lung secondary to demonstrable bronchial foreign bodies.

From an etiologic standpoint, the group was subdivided as follows: abscess of the lung following tonsillectomy, seventy-seven cases; abscess of the lung following operations other than tonsillectomy, twelve cases; abscess of the lung following extraction of teeth but in which no foreign body could be found, eight cases, and abscess of the lung complicating acute infection of the lower respiratory tract, thirty cases. In the group of cases of abscess following tonsillectomy, a series of fifty-eight cases that was reported in a previous paper is included.¹

Of the 127 cases, the lesion involved the right lung in seventy-five and the left lung in fifty; there was bilateral involvement in two cases.

Monolobar involvement occurred in 104; two lobes were involved in twenty-one; in the bilateral cases three lobes were involved. The lobar distribution is shown in table 3.

The lobar distribution in the post-tonsillectomic cases corresponds closely to that reported in a previous series. It is interesting to note that of the twelve postoperative cases (extra-oral), eleven involved the right lung.

In this group, six patients are still under bronchoscopic treatment. In 121 patients, bronchoscopic treatment was discontinued because of complete recovery, improvement, lack of improvement, reference to the surgeon for external drainage, or death. The following tabulation is based on the results obtained in 121 cases: well, sixty-six (54 per cent); improved, sixteen (13 per cent); no improvement, eight (6 per cent); referred to surgeon, twenty-eight (23 per cent), and died, three (2.4 per cent).



Fig. 3—Roentgenograms of a patient, aged $3\frac{1}{2}$ years, admitted to the Chevalier Jackson Bronchoscopic Clinic, Jefferson Hospital, because of high fever, persistent cough and some difficulty with breathing. There was a history of pneumonia (?) four months before admission. The child was extremely ill; fever was septic in type, at times reaching 106 F., there was marked anemia, hemoglobin being 32 per cent and red blood cells 2,300,000 per cubic millimeter. *A* is a roentgenogram made on admission of the patient by Dr. W. F. Manges, who reported as follows: "There are multiple foci of suppuration in both lungs. The middle and lower lobes are involved on the right side and the upper lobe is involved on the left side. There is evidence of cavitation." Bronchoscopy was advised and aspiration was instituted with definite improvement. A total of eight bronchoscopic aspirations were carried out during a period of twenty-six days. *B* was made five days after the last bronchoscopic aspiration; no evidence of cavity formation was found, and slight peribronchial thickening remained. The patient was discharged well.

The best results are obtained when bronchoscopic treatment is instituted early in the disease. Jackson, McCrae, Meyer and others have repeatedly stressed this point. Its importance is well demonstrated in these cases. Of the entire group of 121 patients, sixty-two (51 per

cent) were treated bronchoscopically within three months after the onset of symptoms. Of these, forty-four are well, nine were referred to the surgeon for external drainage, six are improving, one remained unchanged and there were two deaths. This gives a recovery rate of 70 per cent. It is probably true that certain of these patients would have recovered spontaneously under medical care alone. It may be recalled, however, that the majority of the patients referred to the bronchoscopic clinic for treatment had been under medical care for a time, and it was the opinion of their medical advisers that bronchoscopy should be instituted, presumably because of the lack of sufficient improvement to warrant continuation of medical treatment alone.

In a comparative analysis of the cases referred to the surgeon and those in which bronchoscopy has been successful, nothing unusual was observed so far as lobar distribution of the suppurating process was concerned; nor was there any remarkable disproportion between the ages of the patients in the group of cases occurring after operative

TABLE 3—Lobar Distribution

	Monolobar Lesions		Multilobar Lesions	
Right upper lobe	37	Left upper lobe.	23	
Right middle lobe	4	Left lower lobe	19	
Right lower lobe...	21			
Right upper and middle lobes	2			
Right lower and middle lobes	11			
Bilateral involvement	2	Left upper and lower lobes..	8	

procedures. In the cases of abscess following infections of the respiratory passages it was noted that the average age of the patients referred to the surgeon was 41 years, as compared with 34 years, the average age of patients who recovered following bronchoscopy.

An important consideration in treatment is the avoidance of exposure of the patient to acute respiratory infections. In four instances, patients who were considered practically well were discharged from the hospital at a time when, unfortunately, acute infections of the upper respiratory tract were prevalent. Each of these patients contracted an acute cold, and subsequently there was reinfection with recurrence of the pulmonary lesion (fig. 4). In three of these, bronchoscopic aspiration was again instituted but without benefit, and they were referred to the surgeon for external drainage. In the remaining case, bronchoscopy was contra-indicated by reason of pleural involvement.

SURGICAL TREATMENT

The indication for surgical intervention is the failure to bring about a cure within a reasonable length of time by the more conservative measures. In a small percentage of cases when the patient first comes

under observation, the abscess is so close to the wall of the chest that it is safer to resort at once to external drainage than to risk the development of an empyema. The type in which the abscess cavity has a markedly fibrosed wall will probably always require operation, but nothing is lost and often a great deal gained by bronchoscopic drainage and other conservative measures until the maximum benefit of such treatment has been obtained.



Fig. 4.—Roentgenograms of a man, aged 29, who developed pulmonary symptoms following tonsillectomy under general anesthesia. He was admitted to the bronchoscopic clinic for treatment six weeks after onset of symptoms. *A* is a roentgenogram made on admission of the patient to the Jefferson Hospital. There is an abscess in the posterior portion of the upper lobe of the left lung. Bronchoscopic aspiration was instituted with satisfactory results. After nineteen treatments were given, cough and expectoration were negligible, and the chest seemed clear. *B* was made just before the patient was discharged. The inflammatory changes in the left upper lobe have almost completely cleared up. *C* was made two months after discharge from hospital. There has been a recurrence of the pulmonary infection with extensive changes in the upper lobe. Bronchoscopic treatment was again instituted without benefit. Surgical drainage was carried out with complete recovery of the patient.

In the group of twenty-nine patients operated on, bronchoscopic treatment had been tried unless contraindicated or unless operation was clearly the procedure of choice. We have not considered the duration of the abscess as a prime determining factor in the selection of the method of treatment, since some cases of long standing have responded to bronchoscopic drainage, while others of but four or five weeks' duration have required operation. The shortest duration of the disease in the group of patients treated by external drainage was four weeks. The average duration in all the patients thus treated who made complete recoveries was five and eight-tenths months; in those who died, seven and three-tenths months.

The selection of the proper time for operation is important. This has been stressed by Miller and Lambert,⁴ who believe that external drainage in the acute phase of the disease is extremely dangerous. In some of their cases in which the abscess was opened during this stage there followed a wide extension of the pneumonic process with a fatal termination in from three to seven days. At autopsy, they found "a widespread massive involvement of the entire lung or both lungs, in which the bronchi were filled with pus and the alveoli either showed the changes of an acute pneumonia or were swollen, edematous and infiltrated with leukocytes. In some cases there were multiple small abscesses widely disseminated throughout the lungs."

In two of our fatal cases in which the patients were extremely ill and had large abscesses involving an upper lobe, we had a similar experience—improvement for a few days, then the development of small abscesses disseminated throughout both lungs.

Miller and Lambert were of the opinion that external drainage does not drain the pneumonic process about the central suppurating focus which is present during the acute phase, and that with the establishment of a free opening, the effectiveness of coughing to empty these areas is greatly reduced. With this, we are in accord.

After the abscess has been localized as accurately as possible the exposure is planned, keeping in mind a two-fold object, namely, drainage and obliteration of the cavity. In cases of short duration, obliteration of the cavity will probably take place if adequate drainage is established and maintained for a sufficient length of time, the expansion of the lung and contraction of scar tissue making any plastic procedure unnecessary. Cases of long standing require a more formidable procedure in order to obtain obliteration of the cavity.

As a general proposition an abscess of the upper lobe can best be reached through the anterolateral wall of the chest. In three of our

4. Miller, J. A., and Lambert, A. V. S.: Treatment of Abscess of the Lung, *Am. J. M. Sc.* 171:88 (Jan.) 1926.

cases a posterior approach was used, dividing the rhomboid muscles and pulling the scapula outward. In one of these it was evident at operation that an anterior exposure would have been better, as the abscess cavity sloped downward and forward, and this was done subsequently. In the other two the abscess probably could have been reached just as well through an anterolateral incision. It is our feeling that the posterior approach in abscesses of the upper lobe is seldom advisable. In abscesses of the lower lobe the approach is posterior or posterolateral and in abscesses of the middle lobe, anterolateral.

With increasing experience, our views regarding the proper procedure in the surgical treatment for pulmonary abscess have undergone certain changes. We are no longer content with simple drainage in the majority of cases, but believe that something more must be done if a complete cure is to be obtained. Obliteration of the abscess cavity depends on contraction of its wall, as well as on expansion of the lung. This cannot occur in large, superficially located abscesses while part of the abscess wall is held out by the rigid framework of the chest. It is therefore necessary to resect a sufficient portion of the ribs near the abscess to permit this contraction to take place. Three or four inches (7 or 10 cm.) of two or more ribs, depending on the size and location of the abscess, should be subperiosteally resected and then the corresponding intercostal muscle bundles, with the periosteum of at least one rib, removed. Separation of these structures can be simplified by cautiously incising through an intercostal muscle bundle until the line of cleavage is found. In two of our cases the pleural cavity was accidentally opened, but no harm resulted other than the delay of the final stage of the operation.

In this group of twenty-nine patients operated on, nineteen (65.5 per cent) had obliteration of the pleural space in the region exposed. Eight (27.5 per cent) had light adhesions and only two had an uninvolved pleura (6.8 per cent). In none of the cases has suturing been done to bring about the adhesion of the pleural surfaces; dependence has been placed on the irritation of an iodoform gauze pack left in situ for about a week. Empyema occurred in one case. At autopsy there was found, in addition, an acute bronchopneumonia and a diffuse peritonitis. This patient had an abscess of the upper lobe and as far as it was possible to determine at postmortem examination there had been no leakage from the abscess into the pleural cavity.

In fourteen of the twenty-nine patients operated on, drainage of the abscess was accomplished at the primary operation. In recent cases we have been more radical and believe that the final results are better. With ample exposure of the area involved, one can work with greater safety. Whenever possible, a large part of the outer wall of the abscess has been removed. In one instance, a small abscess of the middle lobe

was practically excised in two stages. At the first stage the outer wall was removed with the endotherm knife, and at a second stage the remaining wall was taken away. There was remarkably little bleeding except from the vessels which accompanied the small bronchi and these required ligatures. We believe that the endotherm knife is destined to play an important part in the development of thoracic surgery.

As soon as the abscess is opened it is emptied of its contents to avoid the aspiration of pus into other parts of the lung. One can then explore to determine the extent of the lesion and remove as much as possible of the outer wall. It is sometimes wise to be content with drainage at first and to remove or destroy the wall of the abscess later. Removal or destruction of the wall of the abscess has been accomplished in this group of cases with the endotherm knife, with the electric cautery or with the soldering iron after the method of Graham.⁵ A cavity which at first is large soon shrinks if there has been sufficient resection of the ribs over it and an adequate opening made for drainage.

We have discontinued the use of drainage tubes except when we wish to establish a permanent bronchial fistula, and then only after the external wound has partly closed. The cavity should be packed with gauze which, while it permits drainage, obstructs the opening sufficiently to enable the patient to cough effectively and bring up material from parts of the lung not drained through the abscess cavity. This we believe is important in lessening the occurrence of a large pulmonary complication which sometimes follow closely the free opening of a large abscess.

In no case have we had secondary hemorrhage or experienced bleeding at operation which was not easily controlled by packing. An ample exposure and a large opening in the abscess cavity lessen greatly the danger from hemorrhage.

In fifteen cases, the abscess was drained at a second stage. The wound was packed with iodoform gauze, and further roentgen studies were made to establish the relative position of the abscess to the area from which the ribs had been removed. We observed that temporary improvement often followed the primary operation, probably due to the compression made by the pack.

Subsequent operations were required in ten cases either because of multiple abscesses or because the primary operation failed to bring about recovery. Some of these patients were operated on a number of times. Where obliteration of the abscess cavity has not kept pace with healing of the wound, we have excised the scar, again exposed widely the diseased area and cauterized it thoroughly. In some instances, it

5. Graham, E. A.: *Rôle of Surgery in Treatment of Pulmonary Suppuration*, J. A. M. A. 85:181 (July 18) 1925.

has been necessary to remove regenerated rib; in some the entire procedure has had to be repeated several times, but each time the cavity has been smaller, and finally the remaining fistulas have spontaneously closed as the wound has healed.

We have used local anesthesia alone in nineteen cases, local in conjunction with nitrous oxide anesthesia in eight cases and nitrous oxide or ethylene anesthesia alone in two cases. We prefer local anesthesia alone or local anesthesia with nitrous oxide analgesia to general anesthesia because it is safer not to abolish the cough reflex. With local anesthesia and nitrous oxide analgesia, if the patient wishes to cough, the mask is removed and the operation momentarily suspended. Morphine and atropine are given by hypodermic injection half an hour before the time set for operation.⁶

There were ten deaths in the group of twenty-nine cases (34.5 per cent). This mortality may seem high, but we have not refused to operate on any patient, however ill, if operation has offered any hope. Two died from cerebral embolism which occurred during the course of operation, one under local and the other under general anesthesia. In the former, death occurred suddenly as the operation was being completed. In the latter, a hemiplegia occurred during operation and death took place within twenty-four hours. Abscess of the brain was the cause of death in three patients, two of whom were regarded as doing well at the time of the development of this complication. Two died from multiple small abscesses disseminated throughout both lungs; one from acute bronchopneumonia (autopsy); one from acute bronchopneumonia, empyema and peritonitis (autopsy), and one from the development of an abscess in the other lung with rupture into the pleural cavity and a pyopneumothorax.

It is interesting to note that in this group of twenty-nine cases, nineteen (65 per cent) had the abscess located in the upper lobes, and eight of the ten deaths (80 per cent) occurred in patients having involvement of the upper lobe.

Two patients developed a recurrence of the abscess. In one, it recurred more than two years after apparent recovery, during which time the wound was healed and the patient was practically free from symptoms. This man originally had three abscesses, all showing fluid levels. Two abscesses in the right upper lobe responded to bronchoscopic drainage and have remained cured (fig. 5A and B). The abscess of the left upper lobe was operated on and apparently cured; but it has recently recurred (fig. 5C). The second patient had an abscess of the right lower and middle lobes; both were drained. A permanent bronchial fistula was established in the right middle lobe. He worked

6. Flick J. B.: Lung Abscess, *Ann. Surg.* 84:323 (Sept.) 1926.

as a machinist's helper for seven months, then developed a recurrence of the abscess in the right lower lobe. He was again operated on and a permanent bronchial fistula established in the lower lobe. He is now free from symptoms and working as a gardener, but he has two permanent bronchial fistulas. Nine patients (31 per cent) made complete recoveries. Two of these required multiple operations. Three patients recovered with bronchial fistulas, but are free from symptoms and working. This makes twelve patients, or 41.3 per cent, who have

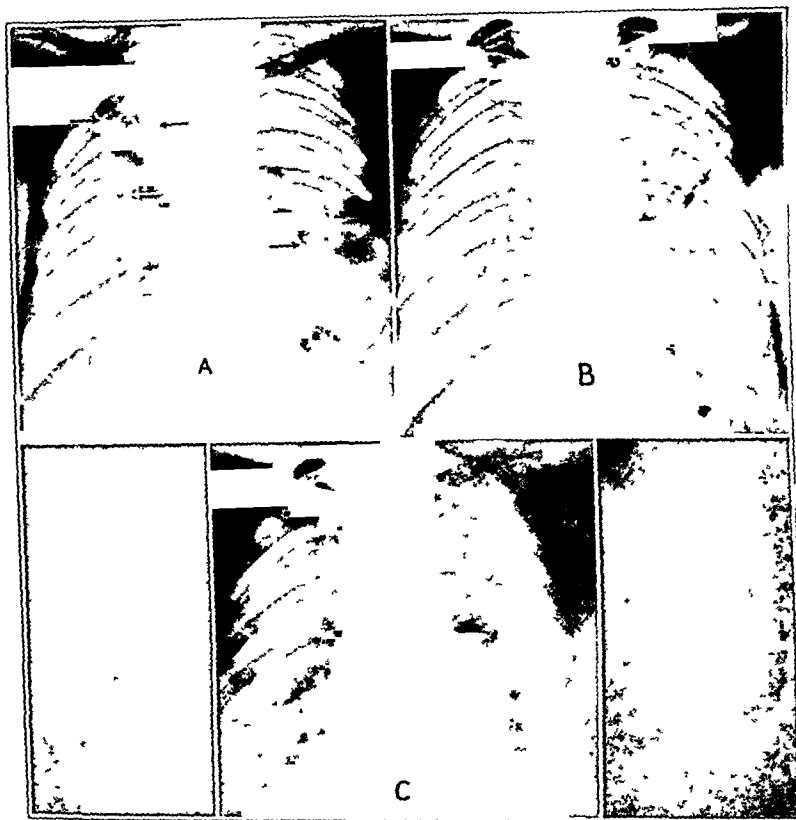


Fig 5—Post-tonsillectomic abscess of the lung with multilobar involvement. *A*, a roentgenogram made on admission of the patient to the Jefferson Hospital, shows abscess cavities with fluid levels in the upper and middle lobes of the right lung and in the left upper lobe. Bronchoscopic treatment was instituted, the right lung cleared, but the area of infection in the left lung increased. External drainage was performed with apparent recovery. *B* was made about two years after discharge of the patient from the hospital, both lungs are clear and the patient is clinically well. *C*, made five months after *B*, shows recurrence of the abscess at the base of the left upper lobe. The right side has remained clear.

returned to work. Two patients are improved, but because of bronchiectasis will require thoracoplasty. One of these developed

bronchiectasis as a sequel to a pulmonary abscess (fig. 1); the other developed an abscess as a complication of bronchiectasis (fig. 2). Four are improved but are still under treatment. One patient is unimproved.

CONCLUSIONS

The diagnosis and treatment of abscess of the lung requires the close cooperation of internist, roentgenologist, bronchoscopist and surgeon. The prognosis in a given case is often favorably influenced by the teamwork of this group. A diagnostic bronchoscopy should be done in all cases of pulmonary abscess irrespective of the method of treatment to be employed. The sine qua non in treatment is the establishment of adequate drainage. This may be accomplished in many cases by conservative measures which include repeated bronchoscopic aspirations. The indications for surgical treatment have been outlined. Conservative treatment should not be continued too long if distinct benefit is not obtained, since complications occur which increase the risk and decrease the chances of recovery with surgical intervention.

A CASE OF ABSCESS OF THE LUNG WITH FILLING OF A CAVITY AND CLOSURE OF A BRONCHIAL FISTULA BY PEDICLE MUSCLE GRAFT

FRANCIS A. C. SCRINGER, M.D.
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REPORT OF A CASE

History.—F. B., a woman, aged 27, was admitted to the Royal Victoria Hospital on Feb. 11, 1929, where a diagnosis of abscess of the upper lobe of the right lung was made. She was first admitted to the medical service in August, 1928, with a diagnosis of tuberculosis of the right upper lobe. After investigation this was changed to abscess of the lung of nontuberculous infection. She complained of cough and foul-smelling sputum; pain in the right side of the chest and a dull ache at the level of the spine of the scapula. She dated the illness to a period following tonsillectomy, which was performed under general anesthesia. In August, 1928, two days after the operation, she suffered from a sharp pain under the scapula. One week later, she began to expectorate foul-smelling sputum. The quantity of sputum increased to 2 or 3 ounces of pus in twenty-four hours, which was usually blood-stained.

Examination.—On examination, there was evidence of consolidation of the right upper lobe. Roentgen examination revealed a cavity in this area which partially filled with iodized oil 40 per cent.

Operation and Course.—On February 14, under local and gas oxygen anesthesia, an incision was first made in the axilla, and a portion of the third rib was removed. Here the pleura was found thin and not adherent. The wound was then closed, and a second incision was made in the back. Portions of the third and fourth ribs were removed. Here a manometer needle showed no excursion during respiration. The pleura was incised with a high frequency knife, and a cavity in the apex of the lung was entered through thickened, firm lung tissue. The extreme apex of the lung was soft. The cavity was widely opened with the high frequency knife and was found to communicate with a large bronchus. The cavity was packed, and the wound was left open.

Following this operation, the sputum cleared and the temperature became normal. The packing was removed on the third day, leaving a cavity situated under the scapula with a large bronchial fistula opening into the inner wall. This was dressed until March 18, 1929, when the superficial wound tended to close, leaving a considerable cavity.

On March 18, with the patient under gas oxygen anesthesia, the previous wound was excised. The cavity was found to be about the size of a hen's egg; in the depth was a fistulous opening large enough to admit a lead pencil. The wall, while tense, was not hard and felt elastic. It was therefore felt to be wise not to cauterize further. The simplest way to obliterate the cavity appeared to be by turning in pedicle muscle flaps, and two of these were fashioned, an upper one from the uncut part of the rhomboid with its pedicle to the upper medial side. It was about 2 inches (5 cm.) long. A lower flap of about the same length was made from the cut portion of the rhomboid. When these were turned in,

they completely filled the cavity. A small rubber drain was put underneath them to act as a path for discharges from the cavity. The rest of the wound was partly closed.

The patient left the hospital on April 16 apparently well. The wound was closed. There was no sputum.

COMMENT

This is merely a preliminary report the only interest of which lies in the apparent closure of a considerable cavity associated with bronchial fistula.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. HOLMAN AND MATHES; VAN ALLEN AND ADAMS;
FLICK, CLERF, FUNK AND FARRELL, AND SCRIMGER

DR. ELLIOTT CARR CUTLER, Cleveland: By utilizing his previous experiences and knowledge of circulatory phenomena, Dr. Holman has brought a new aspect to the study of pulmonary suppuration.

Chief interest heretofore has been focused on the actual mechanism by which the suppuration is produced, whether aspiratory or embolic; or it has concerned the matter of the bacteriologic agents in the abscess of the lung, whether anaerobic or aerobic.

Now Dr. Holman brings a study of the intimate vascular supply. It would seem that in considering this matter from this point of view we will get certain new and instructive attitudes toward this problem which will be of value to us. Pathologists have long pointed out that the differentiation between gangrene and abscess depends to a certain extent on the occlusion of the vessels. Gangrene seems to occur only when both the pulmonary arterial supply and the bronchial arterial supply is cut off.

I should be interested in asking Dr. Holman whether he had the opportunity to study the bronchial artery in any of the animals in which he had produced suppurative lesions and whether the patency of this vessel bore any relation to the type of lesion produced, i. e., gangrene or abscess. If he has not done this, I would suggest that it might be worth while to produce gangrene by the use of ordinary mouth anaerobes and see whether there is not a difference in the vascular supply.

The other lesson he brings to us is that most instructive point of the enormous collateral circulation that can come through the bronchial artery. I think all thoracic surgeons will be interested in that observation. His injection studies have demonstrated the enormous capacity for adaptation and reserve which is afforded here as elsewhere in the body.

DR. EMILE HOLMAN, San Francisco: We have not used the anaerobic organisms. The same three organisms were used throughout, and were kept under a constant condition of virulence by subculture. We, therefore, thought we were getting a comparable picture in each instance from an infecting organism of constant virulence.

DR. WILLY MEYER, New York: These presentations prove that we all have learned from the pathologist long ago, that if an infectious embolus is thrown into the lung local infectious inflammation will take place, except when there is the fortunate combination of low virulence and extraordinary resistance of the system. When the embolic material was sterile, no inflammatory process followed.

I wish to remind you of a patient who had been operated on for varicose veins, and who during after-treatment experienced, with alarming swiftness, partial embolism of the lung. If there had been phlebitis, one would have had to fear gangrene with abscess of the lung; if not, the size of the embolism would decide recovery or rapid fatal issue.

The important question of the usefulness of ligation of the pulmonary artery and its branches in the treatment of patients with pulmonary infections was briefly touched on. In animal experimentation one never sees gangrene of the lung or abscess after such a ligation so long as the work is carried out aseptically. This was observed in the clinic. One must remember that the pulmonary artery is a functional, not a nourishing, blood vessel, carrying the blood to the alveoli for the exchange of gases. If the pulmonary artery is ligated, the bronchial arteries continue to attend to nourishment of the tissue of the lung. There is no reason why local gangrene should occur so long as perfect asepsis is maintained. In the consideration of this chapter of thoracic surgery it is wise to remember that anastomoses exist between the bronchial arteries and the branches of the pulmonary artery.

The question was stressed whether an abscess of the lung is caused by embolism or by aspiration. I think all of us who have given the question due consideration and observation have come to the conclusion that opposing minds have to compromise. We have to say that both, embolism as well as aspiration, may be the cause. The main point is: What is the percentage of each? This question was raised particularly in New York about ten or fifteen years ago, when a real epidemic of abscesses of the lung was seen following the many tonsillectomies done in the early study of the cure of the so-called focal infections. There was a great number of cases of acute pulmonary infections, and a cry went up from the medical profession, particularly in discussions at the Academy of Medicine, that something was wrong in the method of removing the tonsils. The specialists working in this line quickly took this to heart. Today I can state conscientiously that abscess of the lung following tonsillectomy is a rarity in New York. Why? Because the physicians who do not operate under local anesthesia employ experts for the general anesthesia, who handle electric suction of the fauces to perfection. Can there be a better proof for the claim, that "aspiration" has been the principal factor in the occurrence of abscess of the lung after the removal of the tonsils? I know of one colleague standing high in the medical profession who has had only one case following tonsillectomy in the last fifteen years in the wards of a big hospital. He was so mortified that he personally went to the hospital day and night to see how the patient was getting along.

There is, then, no question but that operations on the tonsils, operations within the mouth, nose and pharynx are the cause of the greatest majority of post-operative abscesses of the lung, and their formation must be principally due to the aspiration in the course of the operation.

Just one word on bronchoscopy, which has come to the fore in this group of cases. Personally, I have always considered bronchoscopy equal to cystoscopy in the diagnosis and treatment of diseases of the urinary system. We all have hailed with delight the use of the ophthalmoscope, the pharyngoscope, the cystoscope and now of the bronchoscope. I believe that we owe it to our thoracic patients with expectoration, to subject them to bronchoscopy, so long as there is no valid contraindication. What an expert sees with his eyes, he sees; his diagnosis stands. Knowing that aspiration of a foreign body so frequently is the cause of suppurating pneumonitis, this fact alone demands the use of the bronchoscope. To my mind it is necessary that every well conducted hospital has a trained bronchoscopist in whose diagnosis the other colleagues can trust.

Suppuration of the lung is also due to cancer. If we take the stand that every case of unexplained persistent cough should be cleared up, if possible, we should insist on having bronchoscopy done on such a patient as soon as possible. Cancer of the lung is most frequently seen in the right main bronchus. Dr. Jackson of Philadelphia treated some patients with this condition years ago. Dr. Kernan, the bronchoscopist of the Lenox Hill Hospital in New York, now has under observation two early cases of cancer of the lung which started in the main bronchus. One case has been cured by local treatment through the bronchoscope; the other is still under observation. I believe that at least nine tenths of the cases of cancer of the lung originated in one of the main bronchi, and that in the majority of these cases, always fatal in former years, there is a good chance of cure being obtained if diagnosis is made early and treatment given locally through the bronchoscope.

DR. HOWARD LILIENTHAL, New York: Solon has said that we must not count any man happy until he is dead, because no one can say what misfortune may happen to him before that time.

Let me call attention to the fact that people with abscesses of the lung are not well merely because they leave the hospital after recovery from operation. In estimating statistics presented here today we must remember that those statistics have to be taken with many allowances; not on account of intentional misrepresentation, but because one cannot tell what is going to happen to a man who has an abscess of the lung and leaves the hospital improved but not normal as, for example, with bronchial fistula. He may be able to work, as it was shown in one or two of the tables, and he is apparently well, except that he has a bronchial fistula. But no one can tell what the final result may be. Many will die of hemorrhages, recurrence of abscess or gangrene or of other septic processes which develop afterward as a result of the bronchial fistula.

Bronchial fistula is only one of the complications I shall mention, because there is not time to go into the discussion of them. I wish to call attention, then, to the fact that in estimating the improvement, including the ability to work, we should count only those persons really cured who have intact chest walls, and in whom the process that led to the abscess of the lung has been eliminated. Those patients who were discharged from the hospital as improved should not be considered well statistically until a long period of time has passed. I have seen deaths occur four, and even five years after the establishment of bronchial fistula, the usual causes being hemorrhage or recurrent pulmonary gangrene and its consequences.

DR. WYMAN WHITEMORE, Boston: I wish to speak for just a minute on Dr. Scrimger's paper.

Two years ago, at the meeting of the American Surgical Association in Richmond, Dr. Eugene Doble showed some lantern slides of a case much like Dr. Scrimger's. He had filled an abscess cavity with muscle flaps, and the patient made a perfect recovery. Patients with chronic abscess of the lung who have been operated on and who have left the hospital with a fistula have been of special interest to me for a long time. Many of these patients do not do well in that the fistulas never heal.

Following Dr. Doble's method, I have operated on five such patients. Some of them had been operated on several times previously; one had had a cautery excision done. One such patient was operated on in Boston last fall before the American College of Surgeons. It was interesting to me to see that a very large cavity such as this one could be completely filled and closed with muscle flap. In all five cases the wound healed solidly and promptly, in about two months. Three of the five patients are well and have no symptoms and raise no sputum;

one patient still expectorates a small amount of sputum but looks well and has gained 30 pounds in weight. Another patient who cannot be considered cured is a woman who had a large cavity from which she had occasional hemorrhages. I operated on her last fall, and closed the abscess cavity with muscle flap. She has done very well, except that she has had one or two small upsets with a little bloody sputum, but these upsets have quieted down while she has been kept in bed.

DR. GEORGE P. MULLER, Philadelphia: My experience has been similar to that of Dr. Flick and his associates, particularly as we have the same close association with the internist, roentgenologist and bronchoscopist. During a period of six years, thirty-five patients with abscesses of the lungs were referred to me for operation. There were ten deaths (28.6 per cent). I want to bring out the point that age makes a material difference in the risk of an operation. The average age of these patients was 36 years, and the mortality of operation in those over 36 years was 44 per cent, whereas in the group below 36 years it was 16 per cent. In eight patients over 50 years of age, the mortality was 62.5 per cent. The mortality in the post-tonsillectomy group was considerably less than in the other, but the average age of these patients was 15 years less than of the other.

A second point concerns the end-results. A number of patients discharged as cured or improved have a relapse and die. In a group of twenty-five patients followed up for at least one year, the final mortality was 40 per cent. Again note the age factor. In the cases in which cure was obtained (at least one year follow-up) the average age of the patient was 32 years, whereas among those who died or improved only, the average was 45 years. Abscess of the lung is a serious disease and only a long follow-up period shows how serious it is.

DR. A. L. LOCKWOOD, Toronto, Canada: I think all of us will concede that operations of all kinds on the nose and throat should be done under local anesthesia. It ought to be the duty of every one of us here to speak continually concerning this to physicians in general, and particularly to internists and the nose and throat specialists. In traveling around the country, one notices that these specialists are still employing general anesthetics in certain cases. They do not want to bother with the nervous, irritable type of girl of about 16 or 17, so they give a general anesthetic. I do not think that the medical profession is entirely cognizant of the incidence of abscess of the lung following operations on the nose and throat done under general anesthetics.

There is one other point, and that is the question of treatment. I do not believe that we ought to be too hurried in the use of the bronchoscope or any radical measure for the treatment of abscess of the lung. Experience has shown us that at least half of these patients are probably cured by postural drainage. If they do not show benefit and improvement under postural drainage, the use of the bronchoscope is indicated.

I would not attempt to argue with the bronchoscopist. We employ him constantly. At the same time, a bronchoscopic examination is not altogether a simple matter. I would much rather have a cystoscopic than a bronchoscopic examination. Dr. Harrington has just brought up a point. He has realized that surgical intervention should not be attempted for at least two weeks after the bronchoscopic examination. I believe that would be the experience of most of us who have operated in many of these cases after bronchoscopic examination. We make it a rule not to do any surgical work until from ten to fourteen days after a bronchoscopic examination.

If the patient is not improved with postural drainage, and with clearing up of all foci of infection, we should do a bronchoscopic examination as a routine.

If the abscess tends to drain following that one examination, we ought to carry on again without the bronchoscopic treatment. We should depend on postural drainage, and use bronchoscopic treatment only when the patients are not benefited by postural treatment.

If these patients are not holding their own, and are not improving with bronchoscopic treatment, we should not delay the surgical treatment too long, but stop the bronchoscopic treatment before bronchiectasis develops, which too frequently occurs after some months.

When it comes to the question of radical surgical intervention, I think that we have to be extremely radical, but that we must use multiple step operations, not doing too much at one time, yet uncovering the cavities widely.

I agree with a previous speaker in regard to tube drainage. I think the abscess cavity should be packed with gauze, fairly firmly, so that there will be some pressure against the open bronchioles, enabling the rest of the lung to be cleared by coughing.

As regards the question of muscle flaps, I do not believe that is altogether a new idea, although it may be a new method of putting them in. They have been tried over some period. If bronchial fistulas are present, I do not believe 100 per cent would be cured by muscle flaps. A muscle flap should not be used over an open bronchial fistula, unless the fistula is exposed and the flap placed adjacent to it. It is necessary to mobilize the cavity so as to allow a collapse about the fistula. After the fistula is closed, muscle flaps should be employed.

DR. ETHAN F. BUTLER, Elmira, N. Y.: Postoperative pulmonary suppuration may be either of embolic etiology or due to aspiration. Dr. Van Allen has indicated the importance of considering a dual etiology.

Prevention of such conditions or the abortion of an impending condition will always be better than a cure. Prevention of suppuration of embolic origin must necessarily depend on the operator's surgical technic. Prevention of suppuration due to aspiration will depend partly on oral hygiene and partly on the ability of the patient to remove infected secretions from the bronchial tree. Therein I believe postoperative hyperventilation by carbon dioxide is of definite value. Increased respiratory effort will clear secretions from the bronchi.

During the past seven years I have seen many patients who, following upper abdominal operations, have been either unwilling or unable to cough up thick tenacious secretions. Within one, two or three days after operation there has been a clinical picture of severe purulent bronchitis, even of impending pneumonia. In ten or a dozen such cases, the purulent secretions have been removed by bronchoscopic methods, and immediately gratifying results have been obtained. The patients have become relieved from distressing symptoms. The temperatures have dropped, and there has been no reaccumulation of secretions with which the patients have been unable to cope. In no case has harm resulted to the recent wound or to the patient.

DR. ELLIOTT CARR CUTLER, Cleveland: Dr. Willy Meyer and Dr. Butler have both emphasized that it is time the proponents of the aspiration and embolic theories tried to get together. I heartily agree with this.

There may be those who think we have overemphasized the embolic theory. We have done this because few paid much attention to the dangers of embolism and seemed to want to blame the anesthetists for their postoperative sequelae, which we felt was unjust.

Dr. Van Allen has just presented a brilliant piece of work. For some time we have tried to superinfect bland emboli by mouth aspiration, in an attempt to correlate both the aspiratory and embolic theories. It was hoped that by freeing

bland emboli which would cause infarction we might then infect these areas from above by mouth organisms. We failed to do this, though Dr. Van Allen has now succeeded.

In his discussion, I wish Dr. Van Allen would point out the type of organisms that were injected in the later contaminations, whether they were pushed down by the bronchoscope or were insufflated, and whether the time interval was a very important factor. If one creates an infarct in the lung or an abscess by the embolic method, these lesions early in their course are not connected with the bronchus. It is difficult for me to imagine exactly how aspirated material gets into the walled-off space and results in chronic abscess. We have no definite criteria to go on.

One insufflation of various types of organisms, whether mouth anaerobes or not, does not usually produce an abscess of the lung, though it is a simple matter to produce abscess of the lung by an infected embolus. Yet we are continually finding that in abscesses of the lung there are many mouth anaerobes. One would like to put these observations together. Experimental abscess is easily created by using emboli infected with mouth anaerobes. Possibly a lightly infected embolus from the operative wound enters the lung and devitalizes the tissue both by reason of the bacteria and the loss of blood supply. When mouth anaerobes are inspired into this area, a chronic abscess is produced.

Although we have failed to do this experimentally, we have observed this sequence of events in clinical cases and utilized this theory for its prognostic value.

Within a year, a patient, aged 27, weighing 200 pounds (90.7 Kg.), was operated on for gallstones. Within two weeks a localized lesion with a fluid level, obviously an abscess, was demonstrated. Also, in a case of ligation of the jugular vein for lateral sinus thrombosis, we observed two abscesses in different lobes within four weeks of operation. The examination showed small, walled-off abscesses with fluid levels. These abscesses were from 3 to 5 cm. in diameter and well walled-off. Both patients had very clean mouths, with only occasional spirochetes. They were given arsenic from the beginning, and we predicted that these lesions would heal promptly if secondary invasion with mouth organisms did not occur; exactly this occurred.

From these observations and from Dr. Van Allen's experiments I think one can predict that small pulmonary abscesses, if the mouth is kept clean and the mouth organisms controlled by arsenic, will not go on to the chronic stage. This would seem to be the practical value of all the experimental work thus far presented.

I do believe that in a great many abscesses, particularly chronic ones, both embolism and aspiration are the causative factors, the aspiration being secondary to the embolus and establishing the chronicity of the lesion.

DR. KENNON DUNHAM, Cincinnati: We have heard a good deal this morning about the bronchoscopic treatment of abscess of the lung. Personally, I should like to know a little more about it. What is the purpose of bronchoscopic treatment of the lung? Is it the aspiration of pus, or is it the washing of the lung as has been recommended in cases of bronchiectasis? I should like to know a little more of what is done with the bronchoscope.

DR. F. A. C. SCRIMGER, Montreal, Canada: I wish to make only one remark. Strictly speaking, it is not a flap that is used, but rather a plug of the muscle in the bronchus. I think that is recognized.

DR. JOHN B. FLICK, Philadelphia: In reply to Dr. Lillienthal's comment, I should like to say that the patients classified as having made "complete recoveries"

have been followed up, and most of them have been heard from within the last two months. The wounds were completely closed, and the patients were free from symptoms.

Of the group of twenty-nine patients treated by external drainage, three were classified as having "recovered with bronchial fistulas." In two of these cases it was a question of either doing an extensive operation or permitting the bronchial fistulas to remain. The three patients when heard from were actively engaged in work; one as a gardener, one as a salesman and the third at school.

In our experience closure of fistulas is best accomplished by excising the old scar, undermining the soft tissues, again exposing widely the diseased area and cauterizing it thoroughly. The fistulas may then at once close with the healing of the wound, or this procedure may have to be repeated a number of times.

DR. LOUIS H. CLERG, Philadelphia: Answering Dr. Dunham's question, bronchoscopic treatment in pulmonary abscess consists primarily in the removal of pus and the improving of drainage; in those cases in which the abscess does not communicate with a bronchus no attempt is made to create a communication, although this is probably mechanically possible. Irrigation is rarely used in these cases; dependence is placed on aspiration with the aid of rigid or flexible, curved or straight aspirating tubes introduced through the bronchoscope into the bronchus draining the abscess.

Dr. Butler's cases recall to mind similar cases referred to us by Dr. W. E. Lee; in these we believe there was atelectasis of the lung. By bronchoscopy, a considerable quantity of thick, tenacious secretion was removed.

Bronchoscopy should be used early in the treatment of patients with abscess of the lung. It is, of course, a question whether it should be performed on acutely ill, septic patients who have diffuse pneumonitis. Skilfully performed bronchoscopy can be considered safe for all practical purposes. Because of this, I know of no sound reason for delaying bronchoscopy to see what will happen to the patient. The frequently observed remarkable improvement following one or two bronchoscopic aspirations in very ill patients is sufficient justification to warrant this assumption.

I agree with Dr. Lilienthal's reference to statistics. Medical statisticians are said to have little regard for the facts. We have tried hard to be fair with ourselves and with those who read these statistics. In so doing we have accepted the only method of expressing our results.

DR. C. M. VAN ALLEN, Chicago: In reply to the kind remarks of Dr. Cutler, I may say that three different sputums were used for inoculation in these experiments; one contained many spirochetes of Vincent, the second, *Fungus nocardia*, which organism is capable of producing extremely chronic suppurative lesions in man, and the third nonspecific, pyogenic bacteria. The ordinary cultural methods and stains were employed in identifying the organisms.

The reason why we succeeded in lengthening the healing time of abscess of the lung by intrabronchial inoculation, whereas Dr. Cutler's associates failed, was probably the one he has given, i. e., that we waited until the tenth day to superinoculate, when the abscess had reached its maximum size and acquired bronchial communication. Such communication would appear to be a necessary factor. There is no other way that I can see for these organisms to reach the abscess.

We believe that superinoculation of the bronchial tree and associated ulcerative lesions of the lungs occurs more frequently than is commonly supposed. A considerable mass of clinical and experimental evidence to support this belief exists and is not generally taken into consideration. For instance, Iglaue, examined the lower respiratory tract for blood after tonsillectomy performed under local anes-

thesia and found contamination in 75 per cent of his cases. Ochsner noted the same thing. He also gave patients who had received procaine hydrochloride anesthesia in preparation for tonsillectomy a few cubic centimeters of iodized oil to swallow, and found that the oil was aspirated in every case. Thus, in using local anesthesia we are not avoiding contamination of the lower respiratory tract in operations on the throat. Moreover, the ease with which any bland fluid accumulating in the unanesthetized pharynx overflows into the larynx and reaches the bronchi is strikingly illustrated by the method of Dr. Singer for intrabronchial introduction of iodized oil. Mucus or mucopus, gathering in the throat during sleep or other time when swallowing is not often engaged in, probably frequently contaminates the trachea and bronchi.

This frequency of bronchial contamination makes the bronchogenic theory of origin of abscess of the lung difficult to understand, without assuming that another factor of lowered resistance plays an essential rôle. And the lowered resistance factor must be a specific circumstance not fully understood, for the usual general and local resistance cannot explain the facts. Thus, the type of patient, above others, in which abscess of the lung is seen is the comparatively well and young person undergoing tonsillectomy; whereas, in operations on the skull, as Dr. Cutler has pointed out, the minimum of postoperative complications of the lungs occurs, although the patients lie under general anesthesia for hours with lowered reflexes and a seriously depressed physical state. What specific circumstance it is of lowered resistance of the lung that prepares it for the intrabronchial inoculation and abscess formation we cannot say further than to suggest that ischemia of a sector of the lung from embolism may be the factor. These experiments show that parenchyma of the lung devoid of its blood supply in large part by an embolus becomes more susceptible to bronchogenic contamination than the normal lung.

DR. EMILE HOLMAN, San Francisco: We too have been investigating the lymphatics of the lung. We find that the injection of the lymphatics over the surface of the lung shows that they lead down directly through the lung tissue to the deeper areas along vessels and bronchus. It is possible that the embolized area may become infected through the lymphatics which drain the bronchus.

POSTOPERATIVE PULMONARY HYPOVENTILATION*

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AND

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The consideration of postoperative pulmonary conditions is of necessity an important one. The fulminant course or the protracted convalescence that follows after such complications forces the question into a major position.

This problem has been approached by many writers (Shultz,¹ Cutler,² Cleveland,³ etc.) after they have gone over large numbers of hospital records and studied the cases listed under pulmonary complications. Carefully planned clinical studies directed toward this condition have been carried out by Whipple⁴ and Elwyn.⁵ Results of these various investigations have helped to clarify the problem in regard to many of the contributing factors in the production of postoperative pulmonary complications. The influence of preexisting pathologic changes, the seasonal variation and the relation of epidemics of infections of the upper respiratory tract to pulmonary complications have been commented on by Ravdin and Kern.⁶ For a long time "ether pneumonia" and the effect of the type and duration of the anesthetic occupied an important place in the literature and was discussed by Robb and Dittrick,⁷ Whipple,⁴ Decker⁸ and others. The importance of direct irritation of the pul-

* From the Departments of Surgery and Roentgenology in the Hospital of the University of Pennsylvania.

1. Shultz: Medical and Surgical Reports of the Presbyterian Hospital, New York, January, 1898.

2. Cutler, E. C., and Morton, J. J.: Postoperative Pulmonary Complications, *Surg. Gynec. Obst.* **25**:621 (Dec.) 1917.

3. Cleveland, Mather: Further Studies in Postoperative Pneumonitis, *Surg. Gynec. Obst.* **27**:282 (March) 1919.

4. Whipple, A. O.: A Study of Postoperative Pneumonitis, *Surg. Gynec. Obst.* **26**:29 (Jan.) 1918.

5. Elwyn, H.: Postoperative Pneumonia, *J. A. M. A.* **82**:384 (Feb. 2) 1924.

6. Ravdin, I. S., and Kern, R. A.: Pulmonary Complications Following Anesthesia and Operation, *Arch. Surg.* **13**:120 (July) 1926.

7. Robb, H., and Dittrick, H.: Pulmonary Complications Following Abdominal Operations, *Surg. Gynec. Obst.* **3**:51 (July) 1906.

8. Decker, H. Ryerson: Postoperative Complications of the Respiratory Tract, *Penn. M. J.* **24**:391 (March) 1921.

monary epithelium and the relation of aspiration to subsequent pulmonary infection has been considered by Bevan,⁹ Herb¹⁰ and Myerson.¹¹

During the past decade the authors writing on postoperative pulmonary complications could be subdivided into three groups, namely, those emphasizing the importance of emboli; those who hold that most complications are due to a pneumonitis, and those who emphasize the frequency of massive or lobular atelectasis resulting from bronchial obstruction.

Cutler and Morton,² in an extensive review of cases, came to the conclusion that embolism was important in the production of postoperative pneumonia. They pointed out the various factors favoring the formation of emboli, such as the presence of septic foci, infection in the operative site, and vessel access to the lungs. They also emphasized the tendency to pulmonary hypostasis resulting from poor expansion due to reflex splinting of the abdomen. Later, Cutler¹² restated his views regarding the embolic theory and substantiated his opinion with roentgenographic studies.

That most of the forms of pulmonary complications are due to a diffuse inflammatory process or pneumonitis has been maintained chiefly by Whipple.⁴ He considered most of the temporary postoperative "reactions" indicative of a mild pulmonary complication and the extension of an acute infection of the upper respiratory tract as the exciting cause. The pathologic change consists principally of vascular congestion and edema with little exudation, and the type IV pneumococcus is the chief organism found. The roentgenograms show a diffuse mottling most marked at the bases, principally the right. This complication occurred in 2.6 per cent of all operative cases in the large series collected by Whipple. Cleveland³ reported a higher percentage of pneumonitis, 33 per cent.

During the past few years, the literature on embolic pneumonia and postoperative pneumonitis has given way to a veritable flood of papers on pulmonary collapse or atelectasis. Although Joerg, as early as 1832,¹³ and Gairdner, in 1851,¹⁴ gave accurate clinical and pathologic

9. Bevan, A. D.: *The Choice and the Technic of the Anesthetic*, Tr. Am. Surg. **33**:21, 1915.

10. Herb, I. C.: *Ether: Simplicity in Its Administration*, J. A. M. A. **66**: 1376 (April 29) 1916.

11. Myerson, M. C.: *Bronchoscopic Observations on the Cough Reflex in Tonsillectomy Under General Anesthesia*, Laryngoscope **34**:63 (Jan.) 1924.

12. Cutler, E. C.: *The Etiology of Postoperative Pulmonary Complications*, Surg. Bull. N. Amer. **2**:935, 1922.

13. Joerg, E.: *Researches on Solidification of the Lungs in New-Born Infants*, Dublin J. M. Sc. **5**:36, 1834.

14. Gairdner, William T.: *On the Pathological Status of the Lung Connected with Bronchitis and Bronchial Obstruction*, Month. J. M. Sc. **11**:122, 1850; **12**:440, 1851; **13**:238, 1852.

descriptions of atelectasis, it was not until the term was revived by Pasteur,¹⁵ Bradford¹⁶ and Scrimger¹⁷ that such a condition was considered in writings on postoperative pulmonary complications. After having recognized atelectatic states in which entire lobes were involved (massive atelectasis), Mastics¹⁸ and his co-workers and Lee and Tucker¹⁹ recently described a patchy or lobular collapse. The occurrence of this type of pulmonary complication after an abdominal operation is even more frequent, according to these reports, than the embolic processes of Cutler or the cases of postoperative pneumonitis of Whipple. Boland and Sheret²⁰ reported 30 cases in a series of 261, an incidence of 11.5 per cent. Mastics and his co-workers¹⁸ concluded that lobular atelectasis comprises 70 per cent of all pulmonary complications.

My associates and I have been engaged in a study of the pulmonary observations of patients before and after upper abdominal operations, and a number of interesting observations have been made. This clinical study was undertaken because the following phases of the subject seemed to need clarification:

1 The frequency of positive reports from the roentgenologic department in patients examined postoperatively in which the subsequent course of events indicated that a pulmonary complication did not exist.

2 The confusion and interchange of terms, such as postoperative pneumonitis, bronchopneumonia, lobular atelectasis, massive atelectasis, "lung reaction," or infarct, these terms being used in describing postoperative pulmonary complications.

3 The marked reduction in vital capacity which was reported by Churchill and McNeil,²¹ and Powers²² following upper abdominal operation.

15 Pasteur, W. The Causation of Postoperative Massive Collapse of the Lung, *Lancet* **1**:1428, 1914.

16 Bradford, J. R. Massive Collapse of the Lung, *Oxford System of Medicine*, 1918-1919, vol. 12, p. 122.

17 Scrimger, F. A. Postoperative Massive Collapse of the Lung, *Surg Gynec Obst* **32**:486, 1921.

18 Mastics, E. A., Spittler, F. A. and McNamee, E. P. Postoperative Pulmonary Atelectasis, *Arch Surg* **15**:155 (Aug.) 1927.

19 Lee, W. E., and Tucker, G. Postoperative Pulmonary Atelectasis, *Atlantic M. J.* **31**:284 (Feb.) 1928.

20 Boland, C. R., and Sheret, J. R. Postoperative Massive Collapse, *Lancet* **2**:111 (July) 1928.

21 Churchill, E. D., and McNeil, D. The Reduction in Vital Capacity Following Operation, *Surg Gynec Obst* **44**:483, 1927.

22 Powers, John H. Vital Capacity, Its Significance in Relation to Postoperative Pulmonary Complications, *Arch Surg* **17**:304 (Aug.) 1928.

4. The limitation of diaphragmatic function as reported by Sise²³ and its relation to the reductions in vital capacity.

5. The presence of preexisting pulmonary pathologic change and its effect on diaphragmatic limitation.

METHODS

Twenty-five cases in which upper abdominal operations were to be performed were studied. No selection of cases as to operative risk, general appearance, etc., was made. None of the patients had any deformity of the chest or gross pulmonary pathologic changes. Cases in which ascites was present were not used. Care was taken that not more than two or three patients were under observation at the same time in order that ample time might be spent in the study of each patient before and after operation.

Daily notes were kept in regard to progress of pulmonary symptoms and physical signs. After operation, the examinations of the chest were made as thoroughly as the condition of the patient permitted. We were able in all cases to examine the bases posteriorly by carefully turning the patients on one side and then on the other.

Measurements of the circumference and expansion of the chest were made before operation and at intervals of two days after operation. The tip of the xiphoid process and the third interspace in the midclavicular line were selected for fixed points for measurement.

Determinations of vital capacity were likewise made before, and at intervals after, operation. The ordinary clinical spirometer was used. The highest of three trials was the vital capacity recorded in each instance.

The patients were studied fluoroscopically in the recumbent and erect postures by the central ray method. The diaphragmatic movements were recorded during quiet (tidal) breathing and during the maximal respiratory phases (deep breathing). The positions of the domes of the diaphragm were marked directly on the fluoroscopic screen with a wax pencil, and these tracings were then transferred to cards for a permanent record. After operation various methods of roentgenoscopy were tried, but the most workable plan and the one which caused the least discomfort to the patients was simply to lift them from their beds to the adjustable fluoroscopic table. With adequate help most patients had practically no pain, and none of the twenty-five, at the time of the examination or later, showed evidences of injury from such a procedure.

Preoperative roentgenograms were made as a routine. After the first four cases were studied it became obvious that the preoperative

23. Sise, L. F.; Mason, R. L., and Bogan, I. K.: Prophylaxis of Postoperative Pneumonia, *Anesth. & Analg.* 7:187 (May-June) 1928.

roentgenogram should be taken in bed in order that this record would be of value in comparing it with the postoperative examinations. In half of the cases studied, roentgenograms were made during the expiratory phase, as well as during the inspiratory phase. In some of the cases in which this study was not made the day before operation, we used for comparison roentgenograms made when the patient returned three months later for follow-up examination. Great care was taken by the technicians to make all exposures with the patients in as near the same semi-Fowler position in bed. Lateral roentgenograms were made in more than half the studies.

RESULTS

The preoperative examination of the patients, from both the clinical and the roentgenologic standpoints, revealed little preexisting pathologic change. However, the importance of the preoperative roentgenograms

TABLE 1.—*Type of Cases Studied*

Operation	Number of Cases	Convalescence Prolonged on Account of Pulmonary Complications	Suspicious Clinical Course	Positive Roentgenograms *
Biliary tract	12	0	2	9
Gastric.	11	1	1	8
Epigastric hernia	1	0	0	1
Splenectomy	1	0	0	1
Totals	25	1	3	19

* The conditions reported as showing positive roentgenograms were postoperative pneumonia, bronchopneumonia, lobular atelectasis, massive atelectasis and pulmonary infarct

when used for comparative purposes with postoperative studies soon became evident. In one case an obliteration of the costophrenic angle due to pleural adhesions was found, which, without the preoperative studies for comparison, might have been interpreted as postoperative pathologic change. We were unable to predict from the preoperative examination of the chest which patients would develop pulmonary complications after operation.

In this series, the operations performed included principally those on the stomach or biliary tract (table 1). The postoperative course was prolonged in one case, this being due to bronchopneumonia. There were no deaths due to a pulmonary complication in the series of cases studied.

The symptoms which suggested a pulmonary complication were few (table 2). Dyspnea and cough were present in only three cases. Hemoptysis of slight amount was reported by one patient. It was in this case that the appearance on the roentgenograms suggested an infarct, and subsequently bronchopneumonia developed on the sixth postoperative day.

Positive physical signs were found surprisingly often in a greater number of these cases than the paucity of symptoms would indicate (table 2). Diminished expansion, especially of the bases, was evident by gross inspection in all of the patients. In four of five patients, suppressed or absent breath sounds were noted over the lower lobes. The diminution in the transmission of sounds was most noticeable at the right base posteriorly. In five of the twenty-five cases, tubular breathing was heard at some time during the postoperative course. Over the same areas, whispered and spoken voice sounds could be heard. These areas over which there was increased transmission of sounds were irreg-

TABLE 2—*Pulmonary Symptoms and Positive Physical Signs*

After Upper Abdominal Operations, 25 Cases		
	Number of Cases	Per Cent
Dyspnea	3	12
Cough	3	12
	2	8
	1	4
	0	0
Positive Physical Signs		
Cyanosis	2	8
	27	100
	8	32
	20	80
	5	20
	14	56

TABLE 3—*Measurements of the Chest**

	Circumference at Xiphoid Process	Expansion	Circumference at Third Interspace	Expansion
Before	79.2 cm	6 cm	84 cm	5.8 cm.
	82	1.3	86.7	1.8
	+2.8 cm	—4.7 cm	+2.7 cm.	—4.0 cm

* This table shows the average changes in measurements of the chest in fifteen of the cases studied before and twenty-four hours after operation. The marked reduction in chest expansion at both points of measurement should be noted.

ular in outline and did not usually appear during the first twenty-four hours after operation, but were elicited thirty-six or forty-eight hours later. Râles were heard in fourteen of the twenty-five patients and were most marked at the bases. The positive physical signs, such as diminished resonance, pectoriloquy and tubular breathing, were evanescent and disappeared in from twenty-four to seventy-two hours as the vital capacity increased.

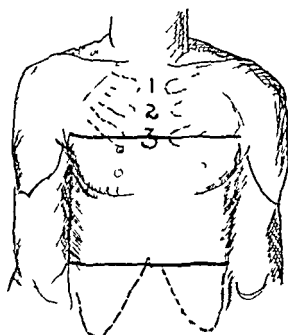
Measurements of the chest after operation in fifteen of the cases showed a marked reduction in the expansion. The average expansion of 6 cm. as measured at the tip of the xiphoid process before operation averaged only 1.3 cm. during the first twenty-four hours after operation (table 3). A similar diminution of expansion was found when the

measurements were taken at a level of the third interspace. The preoperative average expansion was 58 cm., and the day following operation it was found to be only 18 cm. The measurements of circumference of the chest showed an increase following operation, the average being 28 and 27 cm. in the two locations in which the measurements were taken. In figure 1 is illustrated graphically the average alterations in expansion and circumference of the chest as recorded before and at intervals after operation. In table 4 is shown the record in one of the cases. This was selected as showing the typical enlargement of the circumference of the chest immediately following operation and the return to normal size as the convalescent time advanced and the expansion increased.

In only one case in this series was the postoperative circumference of the chest noted to be less than it was in the preoperative record. Mea-

TABLE 4—*Change in Chest Measurements Before and at Intervals After Operation in Case 16 (J. D.)**

	Circum. at Xiph. Proc.	Expan- sion	Circum. at 3rd Intersp.	Expan- sion
PRE-OP.	82 cms.	10	86	11
POST-OP. 1	85	2	89	3.5
DAYS				
3	84	5	87	6
5	84	5	87	6
7	84	4.5	86	8
9	81	7	86	8



* The return to normal circumference and expansion as the convalescent time advanced should be noted. Circumference measurement taken after full expiration. The figure illustrates fixed points selected for making measurements. The patient was a glass blower on whom a gastro-enterostomy was performed.

surements were made in two patients with ascites (not included in this series) on whom a Talma operation was done. In these cases the circumference of the chest was less after operation.

The vital capacity of this group of patients averaged 2,918 cc., which is 75 per cent of the average normal for these patients as calculated by West's²⁴ formula (2.5 liters per square meter surface area for men and 2 liters per square meter for women). On the first postoperative day the average vital capacity was only 33 per cent of the preoperative reading, and the recovery was gradual. Readings taken every second day showed an improvement so that on the eleventh postoperative day

²⁴ West, H. F. Clinical Studies on Respiration, Comparison of Various Standards for Normal Vital Capacity of Lungs. Arch. Int. Med. **25**:306 (March) 1920.

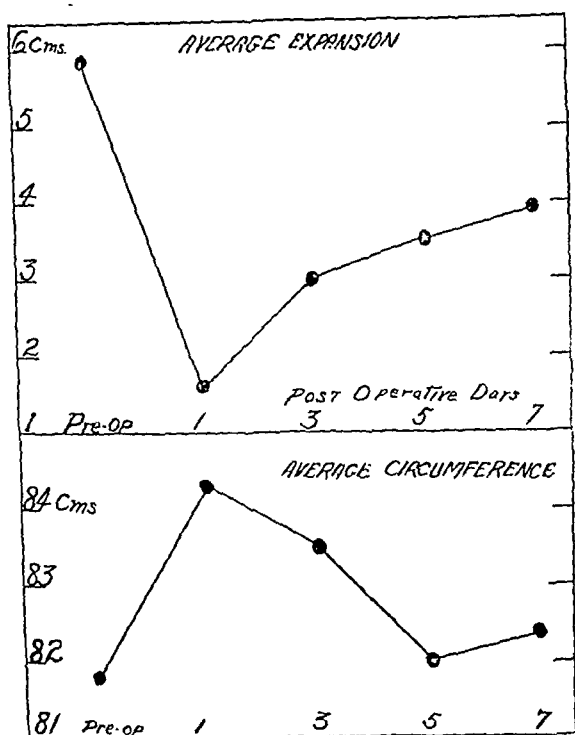


Fig. 1.—Graph showing decrease in the expansion of the chest in fifteen cases after upper abdominal operation. Recovery was gradual and responded to improvement in vital capacity. The increase in the circumference of the chest during full expiration should be noted. Measurements were made at the third interspace and the xiphoid process. A metal tape measure was used.

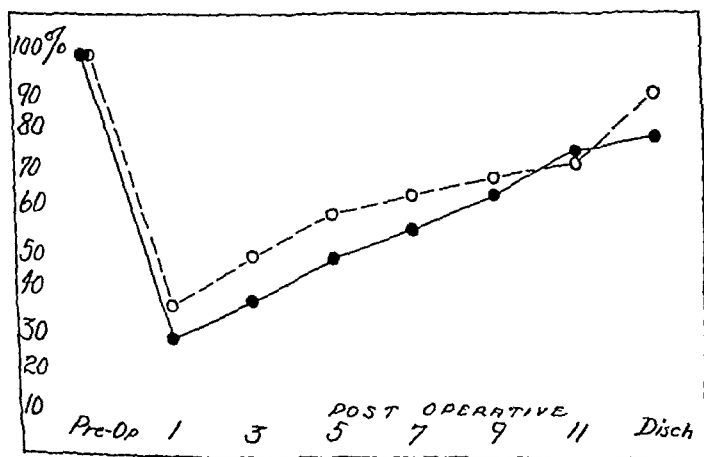


Fig. 2.—Graph showing reduction in vital capacity after upper abdominal operations. Little difference was noted in the average vital capacity records of the six patients in whom the postoperative roentgenograms were clear and in those nineteen cases showing changes postoperatively on the roentgenograms. The solid lines indicate positive roentgenograms and the dotted lines, negative.

an average of 78 per cent of the normal vital capacity was obtained. At the time of discharge, 80 per cent of the normal vital capacity for these patients was the average record. In figure 2 is shown the reduction in the cases, grouped as to whether or not they had positive roentgenologic reports. The significance of these reports is commented on elsewhere in the text. Of the three patients in the group who had frank pulmonary complications, the vital capacity curves were abnormal in two. In one patient (L. M. in table 6) with a complete collapse of the right lung, an average postoperative vital capacity curve was obtained. The maximum fall was 77 per cent, and the recovery was progressively upward. The other two patients (H. W. and F. W., table 6) had the usual initial drop, but the recovery was slow and on the eleventh postoperative day the reading was only 40 and 51 per cent, respectively, of the preoperative record.

TABLE 5—*Diaphragmatic Excursions Before and After Upper Abdominal Operations in Twenty-Five Cases**

	Fullst Inspiration and Inspiration (Maximal)			
	Right		Left	
	Erect	Recumbent	Erect	Recumbent
Before operation	3.4 cm	5.32 cm	3.8 cm	5.48 cm
After operation	1.17	1.6	1.74	1.0
	Quiet Breathing (Tidal)			
	Erect	Recumbent	Erect	Recumbent
	Before operation	After operation	Before operation	After operation
Before operation	1.02	1.24	0.99	1.27
After operation	0.6	0.65	0.79	0.7

* In this table, measurements were made fluoroscopically under uniform conditions before and twenty-four hours after operation.

At the roentgenoscopic examination, an elevation of the domes of the diaphragm was observed in all of the cases after operation. The elevation was most marked on the right side and especially so in two patients in whom later an early massive atelectasis proved to be present. Comparisons in height of the domes of the diaphragms were made from the bedside films. Measurements were made of the perpendicular line dropped from the transverse process of the first thoracic vertebra to a horizontal line through the dome of the diaphragm on each side. The average measurement of the right perpendicular before operation was 25.8 cm. and after, 21 cm., leaving a difference of 4.8 cm., which represents the elevation of the diaphragm after operation. On the left side the perpendicular measurement was 26.5 before and 23 cm. after operation, showing that its position was lower than the right dome and its elevation slightly less (fig. 3).

Diaphragmatic movements before operation were unrestricted in all cases. The maximal excursions were found in the recumbent positions, during both forced and quiet breathing (table 5). It can be seen from this table that in both positions the maximum excursion of the diaphragm

was reduced after operation to a third of its preoperative range of movement. The tidal fluctuations were diminished about one half.

It was also observed that the position of the tidal fluctuation of the diaphragm varied in regard to its position in the maximum range of excursion. Before operation, the tidal movements took place in the lower third of the possible range noted during forced breathing. However, after operation the tidal fluctuations occurred in the upper third of the possible range of movement of the diaphragm.

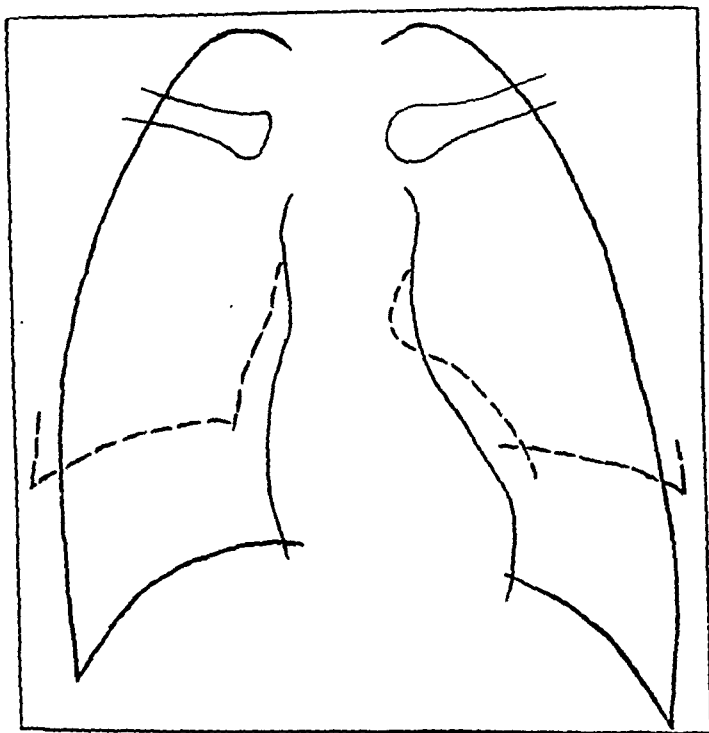


Fig. 3.—Diagram showing relative positions of the diaphragm before and after upper abdominal operations. The marked elevation after operation as indicated by the dotted line should be noted. Measurements were made from roentgenograms taken in the same position during full inspiration. The perpendicular from the transverse process of the first thoracic vertebra to a line through the dome of the diaphragm on each side was taken to indicate the degree of elevation.

		Before Operation	After Operation	Elevation
Average in 15 cases	Right perpendicular..	25.8 cm.	21 cm.	4.8 cm.
	Left perpendicular..	26.5 cm.	23 cm.	3.5 cm.

The alteration in thoracic volume from this factor alone should be noted.

The comparison of the roentgenograms made before and after operation was perhaps the most striking of all observations made in this study. In all of the cases, a definite diminution in volume of the chest

was obvious. There was a narrowing of the inter-rib spaces and an elevation of the domes of the diaphragm. The lung markings were clear in only six of the cases. In sixteen of the cases, there was a marked intensification of the trunk shadows which produced a triangular

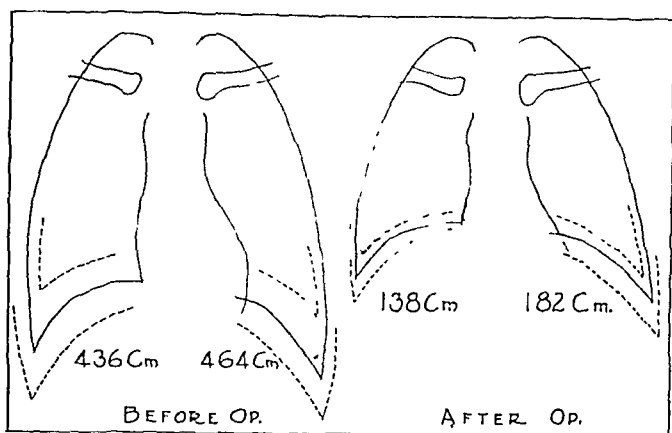


Fig. 4.—Diagram illustrating reduction in the maximal diaphragmatic excursions as averaged from studies in twenty-five cases before and after upper abdominal operations. The patients were studied in both the recumbent and the erect positions. It should be noted that after operation the movements are restricted by two-thirds.

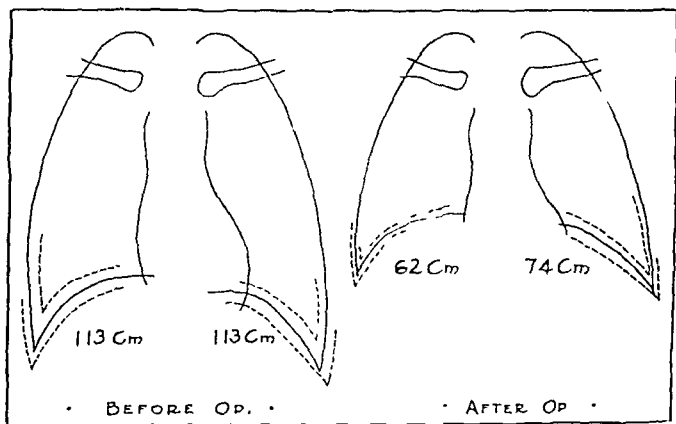


Fig. 5.—Diagram illustrating the limitation of the tidal movements of the diaphragm as averaged in fifteen cases before and after operation and with the patients in both the recumbent and erect positions. It should be noted that the postoperative movements were only one half of the normal.

area of density in the lower lobes. On the right, the cardiophrenic angle was obliterated. On the left, the markings were more or less obscured by the cardiac silhouette. In some of the roentgenograms, there were

varying degrees of haziness or mottling throughout the entire lung fields (figs. 6, 7, 9 and 10).

In the lateral views, the appearance was more striking. The marked reduction in the volume of the chest was clearly evident. The costophrenic angles posteriorly were completely obliterated. The marked diaphragmatic elevation obscured the lung detail in the lower lobes. Air was visible beneath the diaphragm in many of the films (fig. 8).



Fig. 6.—C. W., aged 49. *A*, roentgenogram at full inspiration made before operation for a large, adherent epigastric hernia. The roentgenographic studies in this case are presented because a second-stage pneumoconiosis intensifies the lung markings. *B*, roentgenogram at full inspiration made twenty-four hours after operation. The decrease in thoracic volume, elevated diaphragm, narrowed inter-rib spaces and prominent trunk shadows should be noted. The vital capacity was 25 per cent. *C*, roentgenogram at full inspiration made four days after operation. The partial return of the diaphragm to a normal position and increase in the thoracic volume should be noted. The vital capacity was 85 per cent of the normal.



Fig. 7.—S. H., aged 53. *A*, normal roentgenogram made at full inspiration before cholecystostomy. *B*, roentgenogram made twenty-four hours after operation. The diminished thoracic volume, position of diaphragm and prominent trunk shadows should be noted. This patient had a normal postoperative course. The vital capacity was 32 per cent of the normal.



Fig. 8.—C. D., aged 32. *A*, lateral roentgenogram made before gastro-enterostomy. Bedside position. *B*, study made of same patient twenty-four hours after operation. The size of the aerated pulmonary tissue should be compared with the preoperative roentgenogram. The position of the diaphragm and obliteration of the costophrenic angle posteriorly should be noted. There is a large collection of air beneath the diaphragm. The vital capacity was 23 per cent of the normal.

Roentgenograms made preoperatively during full expiration gave similar appearances to those obtained at examinations made on the first postoperative day. They showed intensifications of the trunk shadows and alteration in the size of the aerated lung (figs. 9 and 10).

It will be noted in table 6 that in sixteen cases a diagnosis of hypoventilation was made. On the roentgenograms, all of these cases showed conditions that would have been diagnosed by us as postoperative pneu-

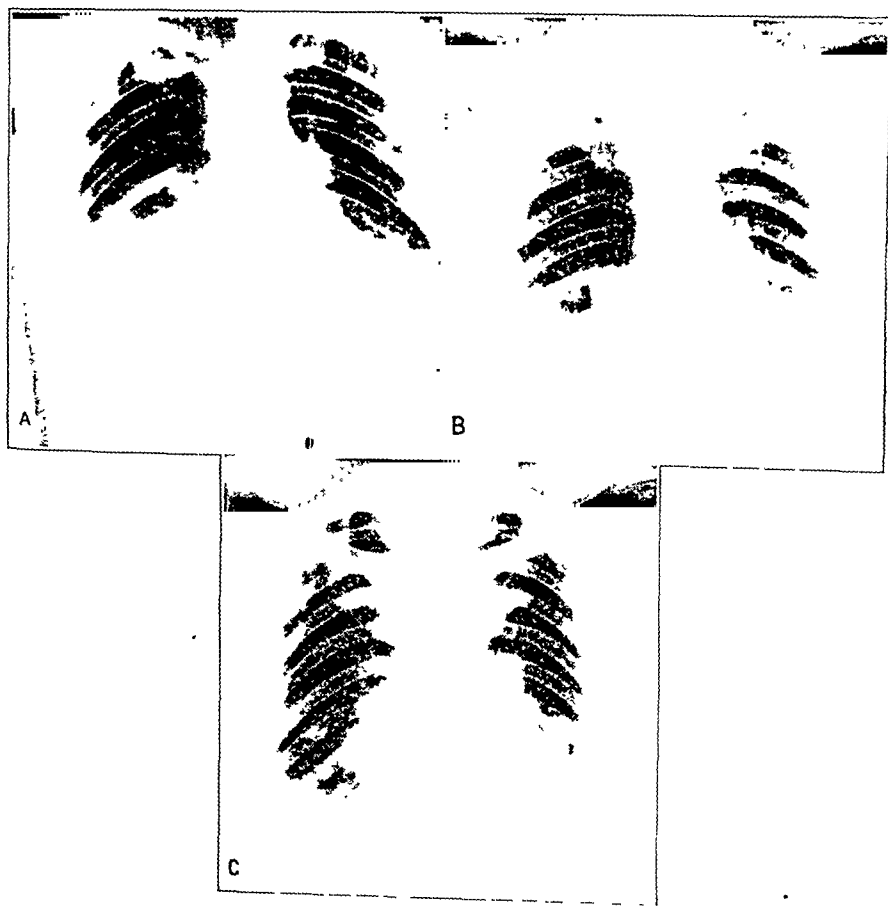


Fig. 9.—L. W., aged 39. *A*, roentgenogram made at full inspiration forty-eight hours after operation (perforated duodenal ulcer). The marked evidences of hypoventilation, the size of the thorax, position of the diaphragm and mottling of the lung fields should be noted. On physical examination of the chest, there was diminished resonance, suppressed breath sounds and later râles and tubular breathing at the bases. The vital capacity was 14 per cent of the reading taken three months later at follow-up study. *B*, roentgenogram made at full inspiration three months after operation. This plate was used as the normal for comparison. *C*, roentgenogram made after full expiration (follow-up study made three months postoperatively). The similarity between this induced hypoventilation and the study made at full inspiration twenty-four hours postoperatively should be noted.

monitis or lobular atelectasis prior to this study. Early in the study, we realized that these appearances (prominent trunk shadows and haziness of the lung fields) were normal postoperative manifestations.

In three of the patients of this series, a major pulmonary complication was demonstrated. In an elderly man, hemoptysis occurred two days after operation for gastric ulcer. The roentgenographic appearance was that of infarction at the right base. The temperature was normal for six days; then it became elevated. Physical signs and roentgenograms showed a diffuse lesion involving the left lower lobe. The patient was placed under an oxygen tent for five days and recovery followed. Both of the other two patients had operations on the gall-bladder. In one, a man aged 60, there were cyanosis, dyspnea and physical signs of lack of aeration in the right lung. Roentgenograms

TABLE 6.—*Reviewed Cases**

Patient	Operation	Excessive Temperature	Excessive Pulse	Post-operative Respirations	Pulmonary Symptoms	Pulmonary Signs	Positive Roentgenogram	Final Diagnosis
L. M.	Cholecystectomy...	+	+	—	+	+	+	Massive atelectasis
H. W.	Gastro-enterostomy	+	+	+	+	+	+	Infarct and bronchopneumonia
F. M.	Cholecystectomy...	—	+	—	—	+	+	Early stage massive atelectasis
Sixteen cases.....		—	—	3	2	16	16	Hypoventilation
Six cases.....		—	—	—	—	3	—	Negative

* In this table, the cases are grouped to show the relation of clinical signs and symptoms to roentgenologic observations and final diagnosis. The three cases which showed frank pulmonary complications are listed separately.

showed haziness of the entire right side. This cleared after inhalations of carbon dioxide, as suggested by Scott and Cutler.²⁵ The other patient in whom a pulmonary complication took place was a woman, aged 23, in whom a cholecystectomy had been done. Following operation, the roentgenogram showed cardiac and mediastinal displacement to the right with little lung density. On the following day, the typical density of massive collapse occurred in the middle and lower lobes. An elevation in temperature; pulse and respiratory rate was noted at this time only. The condition cleared in twenty-four hours, and convalescence was uneventful. This case is being reported separately, in detail.²⁶

25. Scott, W. J. M., and Cutler, E. C.: Postoperative Massive Atelectasis; Effect of Hyperventilation with Carbon Dioxide, *J. A. M. A.* **90**:1759 (June 2) 1928.

26. Overholt, Richard H.; Pendergrass, Eugene P., and Leopold, Simon S.: Postoperative Massive Atelectasis; Report of an Unusual Case, *Surg., Gynec. Obst.*, to be published.

COMMENT

The fact that there is hypoventilation of the lungs following upper abdominal operations has been referred to and commented on by many writers. However, in this study, the various physical measurements of the respiratory movements demonstrate more concretely the extent of this postoperative depression in pulmonary ventilation. The reduction

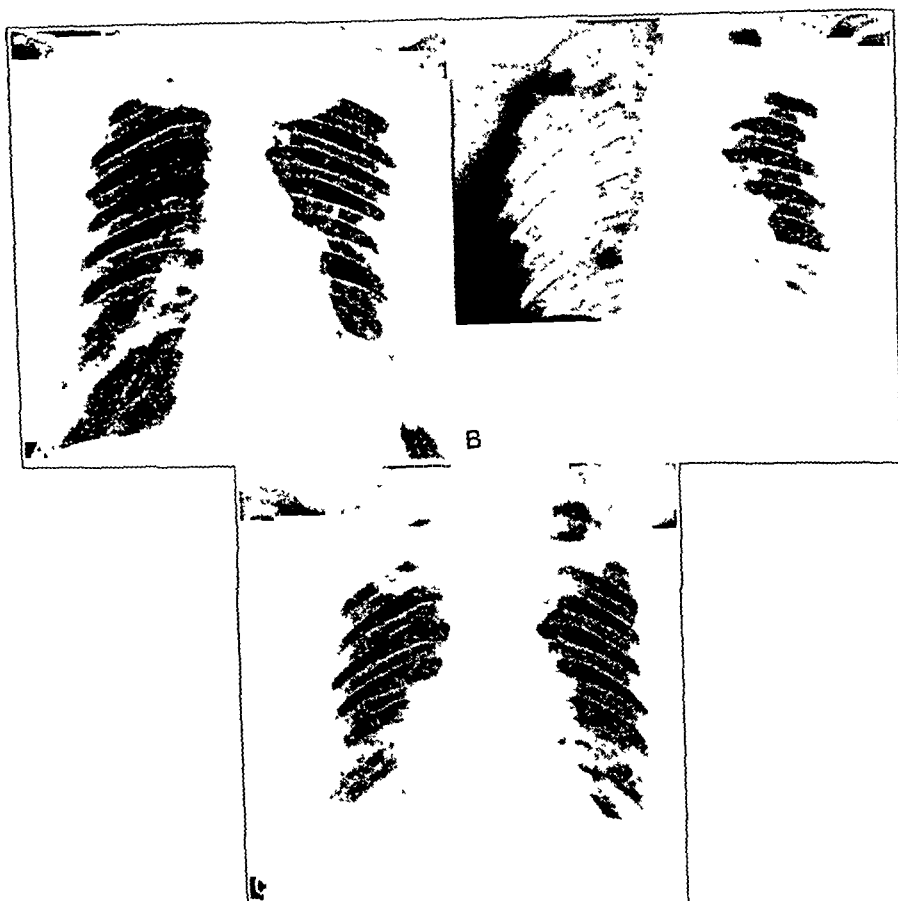


Fig. 10.—A. B., aged 50. *A*, roentgenogram made at full inspiration before cholecystectomy. *B*, examination made the day following operation during full inspiration. The vital capacity was 38 per cent of the normal. *B*, roentgenogram made before operation after full expiration. The similarity of appearances when compared with postoperative study after full inspiration should be noted.

of 79 per cent in expansion of the chest and the limitation of 66 per cent of the diaphragmatic excursions would indicate that a great portion of the reserve of the external respiratory forces was lost for a variable period of time following operation. The constant high position of the diaphragm with the tidal fluctuations occurring in the upper third of its

possible range of motion illustrates the mechanical disadvantage imposed on the diaphragm after upper abdominal operations.

The results of the determinations of vital capacity present further evidence that a state of pulmonary hypoventilation and a marked reduction in the reserve of respiratory function exist. The loss of three fourths of the lung capacity following operations on the upper part of the abdomen was shown both in this series and in reports by Churchill and McNeil,²¹ Powers²² and Head.²⁷ In our experience in cases presenting intrathoracic lesions which were known to be preventing the function of half of the pulmonary tissue, the reduction in vital capacity was no greater than that seen after upper abdominal operations. In this series, the two patients with a massive atelectasis of the entire right lung and the patient with bronchopneumonia and extensive involvement in both lower lobes did not have a reduction in vital capacity which exceeded that in the normal postoperative case.

The number of symptoms referable to the chest in these cases after operation seemed about what would be expected in such a series. From the paucity of pulmonary symptoms, the frequency of positive physical signs seemed abnormally high. However, after considering all of the forces acting to decrease the volume of the pulmonary system and the mechanical difficulties in aerating that portion which is left to function, it is surprising that every case after operation would not present positive physical signs. Even in nonoperative patients who are bedridden, it has been shown that areas at the bases occur over which abnormal physical signs can be elicited. In tuberculous patients, Sewall²⁸ frequently found positive chest signs such as diminished resonance, decreased or absent breath sounds and often râles. Even in normal persons, a physiologic atelectasis may result from a change in posture or in the vigor of respiration. In 1894, Abrams²⁹ referred to a state of atelectasis in the normal lung as well as in pathologic conditions.

Positive physical signs which might be regarded as evidence of a pulmonary complication have been elicited by us after operation and confirmed by the attending internist in a number of private cases, and yet further study and the subsequent course of events showed that the patients were suffering only from the effect of hypoventilation. The type of physical signs depends entirely on the degree of compression and the lack of aeration of the lower lobes.

27. Head, J. R.: *The Effect of Operation upon the Vital Capacity*, Boston M. & S. J. **197**:83, 1927.

28. Sewall, Henry: *Pulmonary Atelectasis as a Source of Confusion in Physical Examination of the Chest*, *Am. Rev. Tuberc.* **4**:811 (Jan.) 1921.

29. Abrams, A.: *Observations on Physiological Pulmonary Atelectasis*, *M. Rec.* **46**:268, 1894.

With what has been said about the frequency of physical signs and the roentgenographic appearance in postoperative studies of the chest, it might seem that the diagnosis of pulmonary complications is difficult. In this series, three patients had frank pulmonary lesions (table 6) which were all distinguishable in the roentgenograms. The two cases of massive atelectasis showed the clinical picture as well. The case in which a diagnosis of bronchopneumonia was made showed the typical temperature chart of pneumonia. The temperature reaction seems the best indication of a frank complication. The respiratory rate and the pulse were not an indication of a complication. The evanescent character of the positive physical signs and the clearing of the lung markings on the roentgenogram as pulmonary ventilation improves would aid in ruling out a postoperative pulmonary complication.

The most interesting and important observation in this clinical study is that most postoperative roentgenograms present an appearance similar to that previously diagnosed as a true inflammatory pulmonary lesion, such as postoperative pneumonitis, bronchopneumonia, or what was considered a pathologic lobular atelectasis. There were only six cases in which the roentgenograms were clearly negative after operation. The other nineteen showed an increased prominence of the trunk shadows at both bases giving a triangular area of density which, on the right side, occupied the inner two thirds of the lung field, and on the left side was largely obscured by the superimposed cardiac shadow. In a few cases there was a mottling at the termination of the trunk shadows which we regarded as evidence of an atelectasis of the primary lobules with or without retained secretions.

In the lateral views, lung detail posteriorly was largely obscured because of the elevation of the domes of the diaphragm after operation.

The degree of the intensification of the trunk shadows and the haziness of the lung fields on the roentgenogram seems to be directly proportional to the degree of elevation of the diaphragm as shown by the perpendicular measurements of the chest. It was thought at first that the degree of intensity of the trunk shadows was determined in part by the type of case studied, i. e., in the short thick chested person the appearance was less striking. However, after reviewing all of the films, it was found that of the six cases in which the appearance was not present, there were four short thick chested patients and two who had long slender chests.

Additional evidence that the postoperative appearance of the roentgenograms is due to pulmonary compression and hypoventilation can be furnished from a comparison of bedside studies made before operation in the expiratory phase and the postoperative examinations made at full inspiration. In many cases, little difference in lung detail could be seen. In some, the diaphragmatic elevation and intensification of the

trunk shadows was more marked in the normal postoperative case than that found in the same case before operation during full expiration.

It has previously been observed that there are changes in the lung markings on the roentgenograms made during full expiration. Machlin³⁰ described shortening and narrowing of the bronchi, principally in the lower lobes. The changes are even more marked when bedside exposures are made. It is the experience of the roentgenologic department of the University Hospital that roentgenograms made in the expiratory phase in the erect posture do not show the marked intensification of the trunk shadows that were observed in this study after bedside examination.

That the evidences of hypoventilation in the postoperative case should be even more marked in some cases than that seen in the preoperative expiratory study can be explained by the fact that this hypoventilation is maintained over a period lasting several hours after operation. This prolonged hypoventilation and compression permit absorption of imprisoned air within partially collapsed alveoli, and true complete atelectasis then is present. The delayed appearance of tubular breathing elicited over these areas could be explained on the same hypothesis—that the maximum density of the atelectatic lung is not reached until the residual air is absorbed.

The observations made in this study lead us to believe that bronchial obstruction, per se, is not the primary factor in the production of atelectasis in the lower lobes after upper abdominal operation. It would seem that the active compression of the lower lobes due to the marked diaphragmatic elevation and the maintenance of this position over variable periods of time, together with the marked reduction in the pumping action of the diaphragm, are all factors which should receive the first consideration. No doubt the bronchi and bronchioles do become obstructed, but we think it results primarily because their lumen become smaller and the air current passing through them becomes stationary.

SUMMARY

1. A definite appearance (a prominence of the basal trunks, haziness of the lung fields and elevation of the dome of the diaphragm) found in the roentgenograms of patients after upper abdominal operations is due to hypoventilation of the lung, and this appearance should be regarded as normal.

2. This roentgenographic appearance is similar to that in cases in which the condition has been diagnosed previously as pulmonary complications, bronchopneumonia, postoperative pneumonitis, or as pathologic lobular atelectasis.

30. Machlin, Charles C.: X-Ray Studies on Bronchial Movements, *Am. J. Anat.* 35:303, 1925.

3. The lung fields on the roentgenogram made at the height of the expiratory phase before operation are similar to those found in the roentgenograms made after operation during full inspiration. Both show evidences of decreased thoracic volume and diminished aeration.

4. Transient positive physical signs in the chest are found frequently after upper abdominal operations. A too hasty diagnosis of a pulmonary complication is not warranted from physical signs alone. Clinical signs and symptoms are of greater value and are usually present when a pulmonary complication exists.

5. Changes in chest expansion and in position and movement of the diaphragm as well as the change in pulmonary volume all explain the marked reduction found in the vital capacity of patients after upper abdominal operation.

6. The varying degrees of partial atelectasis which occur after upper abdominal operations are due primarily to diaphragmatic elevation and restriction.

ABSTRACT OF DISCUSSION

DR. GEORGE P. MULLER, Philadelphia: I have very little to say except that Dr. Overholt has worked hard on this study. We were assisted by Drs. Pancoast and Pendergrass of our roentgenologic department, who have shown great interest in this work on account of the results. This study really started as the result of an argument as to the pathologic condition of postoperative pulmonary complications, because routine roentgen examinations of the chest revealed more pulmonary complications than the clinical evidence seemed to warrant. After some preliminary work had been done, we became aware that there was some discrepancy between the so-called pneumonitis and the clinical aspects. That was the problem Dr. Overholt set to work to try to solve.

He has shown well that after operations on the upper part of the abdomen something occurs to the diaphragm which diminishes the air capacity of the lung, therefore giving an opacity at the base of the roentgenogram which will simulate the pathologic bronchopneumonia or atelectasis.

DR. KENNON DUNHAM, Cincinnati: I should like to inquire why the roentgenograms were always taken on expiration rather than on inspiration.

DR. WILLY MEYER, New York: This highly scientific and extensive follow-up before and after operation by Dr. Muller and his associates is most important.

Many of us have observed postoperative developments carefully from a clinical standpoint. Every older physician remembers, and the younger physicians have had the older ones tell them, that they always were most fearful of the postoperative complications of the lung.

Dr. Muller's study involves surgical work in the upper part of the abdomen, operations on the gallbladder, stomach and duodenum. All surgeons have seen lung complications follow just such operations in spite of a splendidly given general anesthesia as well as after a perfect regional and local analgesia.

From a mere empiric standpoint, my associates and I have been in the habit of advising the patients at the Lenox Hill Hospital in New York to start regular deep inspirations as soon as they have come completely out of the anesthesia. We tell the attending nurses to have these patients practice "gymnastics of the lungs" regularly and faithfully, and we tell the patients that the oftener they do it, the

better it is for them. They close their mouth, then slowly draw a deep inspiration through the nose until it begins to hurt at the seat of operation, and then try to do a little more. In other words, we start the pulmonary ventilation immediately after the operation and explain to the patient that "he has to get rid of the gas still circulating with his blood."

To my delight, I have just heard presented a scientific way of measuring regularly the circumference of the chest and, then, by means of interesting the roentgenographic department in the follow-up after operation, to study the immediate consequences of the operation in the working of the lungs from day to day. It shows "scientifically" the occurrence of the so-called massive collapse of the lung which Dr. Scrimger started discussing seven or eight years ago at the Congress of Clinical Surgeons at Montreal.

The study proves that it is almost a surgeon's duty to insist on this pulmonary ventilation in patients who have had general anesthesia, and the earlier it is done the better.

What causes the massive atelectasis still needs further investigation. I have had some interesting conversations here with a number of men regarding the so-called postoperative massive collapse, better called massive atelectasis. It seems to have been proved by members of the Washington University School of Medicine, by the younger students under the guidance of Dr. Graham, that contraction of the circular muscles of the bronchi evidently plays an important rôle. That seems to be the starting point of the so-called massive atelectasis. Later on, the viscid fluid that collects in the bronchioles and bronchi is added to the original effect of the mechanical contraction of the bronchi. But all this must first be definitely proved.

DR. E. A. GRAHAM, St. Louis: I also wish to add my word of congratulation to these interesting studies. I should also like to commend Dr. Meyer for his apparent success in getting his patients to take deep respirations after upper abdominal operations. I have tried to get patients to do that for a good many years and have not met with any great degree of success.

When Haggard and Henderson published their work about four or five years ago on the use of carbon dioxide for the purpose of washing ether out of the lungs, as they rather graphically expressed it, we began to use the inhalation of carbon dioxide on patients who had had ether anesthesia in a routine manner. Since that time, we have used it almost as a routine for patients who have had any anesthesia, particularly those on whom any kind of abdominal operation has been done. I was also much interested in Dr. Elliott Cutler's article in *The Journal of the American Medical Association* a year or two ago on the same subject, and I agree heartily with everything he had to say.

The difficulty about voluntary hyperventilation is that it is difficult to accomplish. A few whiffs of carbon dioxide, however, will compel the patient to take a deep respiration. We ordinarily start the use of carbon dioxide as soon as the anesthesia is stopped, that is, in the operating room before the wound is closed. Carbon dioxide tanks also are kept in the wards, and the nurses are instructed to give the patients inhalations of carbon dioxide at intervals of about every half hour if the patient is not breathing deeply. If the patient is breathing deeply, then some judgment is exercised by the nurse as to whether it is necessary to give a little carbon dioxide.

It is not necessary for the carbon dioxide to be kept up for any length of time. If the patient takes only two or three deep breaths, it seems to me that this is sufficient to accomplish a proper amount of pulmonary ventilation, enough to avoid massive atelectasis.

At any rate, about three years ago the medical service of the hospital asked, "Why is it you never call us in to see your cases of massive atelectasis? You must have them because everybody else has them."

My reply to that was that we sometimes had patients with high diaphragms, because at about the same period we made observations in about fifteen successive cases of cholecystectomy; when a roentgenogram was taken the next day we found a high diaphragm. These observations were never published.

Since that time, however, the medical service has been actively on our trail. I think that there has been only one case in about three years' time in which there has been anything like a frank, massive atelectasis of the lungs postoperatively. This occurred in a patient who, owing to a combination of circumstances, did not receive carbon dioxide inhalations after the operation.

I feel that this simple device will practically eliminate postoperative massive atelectasis, and that one will not have to depend on voluntary cooperation from the patient, because the patient cannot help taking deep respiration if he breathes a little carbon dioxide.

DR. POL N. CORYLLOS, New York: Dr. Overholt's work confirms the fact that after operations, especially on the upper part of the abdomen, the diaphragm is elevated and the vital capacity decreased. Furthermore, he showed that this decrease was due rather to the impairment of thoracic mobility than to reduction of the thoracic capacity. The elevation of the diaphragm, especially in operations on the abdomen, is due, I believe, to the contraction of the abdominal muscles, reflex as well as voluntary, which is the result of the pain following the operation. Besides, there is always a degree of intestinal paralysis and stagnation of gases in the bowel. Furthermore, contraction and immobilization of the abdominal wall cannot be accomplished without partial, at least, immobilization and splinting of the chest. A unilateral displacement of the diaphragm, however, cannot be explained in the same way. In these cases, in which as a rule, a more or less marked displacement of the heart to the side of the elevated diaphragm will be found if looked for, one should admit without hesitation the presence of atelectasis in the corresponding lung. Atelectasis is not always massive or lobular; most often it is partial. This explains the opacity noticed in the bases of the lungs in most of these cases. It should, however, be borne in mind that even simple compression of the pulmonary parenchyma suffices to give the impression of opacity because of the partial deflation from air of the corresponding portion of the lung. But elevation of the diaphragm alone cannot produce atelectasis as long as the bronchial tree is free. Apneumotosis cannot be produced by phrenicotomy alone. Clinical and experimental data have proved this point, which revived the theory of W. Pateux. I believe that it is time to associate closely atelectasis and bronchial obstruction, and to discard all other proved and provable theories of the pathogenesis of atelectasis, which only befog the question and interfere with its etiologic treatment. Elevation of the diaphragm is one of the several causes (posture, suppression of cough reflex, narcotics etc.) which lead to the accumulation of bronchial exudate in the bronchial tree, especially the most dependent parts of it. But, in these cases at least, there cannot be atelectasis unless there is an obstruction somewhere in the bronchial tree which makes possible the absorption of the intra-alveolar air. I do not deny the existence of lobular bilateral atelectasis of the bases; I will insist only on the fact that elevation of the diaphragm is the result and not the determining cause of atelectasis. Measures capable of increasing thoracic amplification and pulmonary ventilation will oppose the bronchial stasis and will help to prevent atelectasis. Hyperventilation with carbon dioxide acts in that way in preventing or even in curing atelectasis. Henderson, Scott and Cutler have insisted on that

point. In an experimental and clinical work on atelectasis as well as on lobar pneumonia, Dr. Henderson and I obtained interesting results, in which the hyperpnea produced by inhalation of carbon dioxide does not seem to be the only acting cause. It looks as if besides the mechanical action, there is a chemical action of the carbon dioxide inhaled, which may be of practical importance, especially if one bears in mind that, as a rule, the pneumococcus is present in the bronchial exudate in atelectasis.

DR. J. J. SINGER, St. Louis: I was interested in the description of the x-ray reports as given by the essayist. We have often found that the shadows on the roentgenograms are interpreted differently by different men. A shadow in the lung only means a lack of air content, but what causes it is another problem.

In a patient who is on the operating table for an hour or two, perfectly relaxed from an anesthesia and particularly from morphine, it is evident that the dependent parts of the lung would become less ventilated and more congested. Naturally, the lung would fill out less space, and the diaphragm would have to come up to fill out the space.

We have often been surprised to see definite signs of pneumonia in the lung a day or two after an operation, and then to find on the third day that all the physical signs have disappeared.

In 1914, when I first began to study roentgenograms of the chest, I noticed that many of the plates presented by the x-ray department were taken at various phases of inspiration. If one plate is taken today and another two or three days later, they would not look like plates of the same patient. I recall having a roentgenogram made of my own chest at inspiration and at expiration and showing them to my colleagues for their interpretation. A diagnosis of tuberculosis was made from the one taken at expiration. It was purely a matter of lessened expansion, and I think that if every one watches his roentgenograms a little more carefully and interprets them properly, there will be fewer diagnoses of post-operative complications.

DR. RICHARD H. OVERHOLT: Dr. Dunham asked why the plates were taken after expiration. In only about half the cases were plates made after expiration. In all cases, plates were taken at full inspiration. The expiratory films were taken before operation in order to compare them with the postoperative inspiratory plates; both showed hypo-aeration of the lung.

Dr. Graham mentioned the use of carbon dioxide after operation. To all of these patients who received general anesthesia, carbon dioxide was given at the end of the operation. In only one case was carbon dioxide used as well after the patient had been returned to the ward. This was a patient who we thought was developing a massive atelectasis.

Five of these patients were operated on under spinal anesthesia. Most of them were given ether or gas-oxygen combined with procaine hydrochloride locally. The appearance was just the same in cases in which the operation was done under spinal anesthesia; so nothing was said about the type of anesthetic. We feel that the type of anesthetic has no effect on the subsequent appearance of the post-operative roentgenograms.

I was glad that Dr. Singer mentioned the interpretation of the roentgenograms. Early in the study we thought that we were getting complications in all patients, but we later realized it was merely a mechanical change, or cloudiness, as a result of poorly ventilated lung tissue. We feel that this is one of the most important points in this study. We wanted to emphasize the necessity of careful interpretation of the postoperative films. It would be well to check the roentgenograms

made early after operations with those made two or three days later to see whether the same appearance is there.

Dr. Coryllos has called attention to the importance of this whole subject in its relation to the position of the diaphragm. We are now going ahead with this study in an attempt to explain just why the diaphragm does ascend so universally. Atelectasis, to a certain degree, occurs in all these cases in the lower lobes after operation and must be dependent primarily on the position of the diaphragm.

From studies on vital capacity taken from records made after operation, we feel that the pain in the abdomen on the first day will not explain this marked reduction in ventilation, or the 75 per cent reduction in vital capacity. Certainly there is some other factor besides the pain from the abdominal wound that cuts down respiratory activity.

In giving patients morphine after operation and testing their vital capacity at various intervals following such administration, we found that the vital capacity is changed little in those in whom upper abdominal operations were performed. The vital capacity in the patients with lower abdominal operations was greatly improved. In cases of hernia or following appendectomy, the abolition of pain will greatly improve the vital capacity, but will not improve it to such a marked degree following the upper abdominal procedures.

THE CIRCULATION IN THE COMPRESSED, ATELECTATIC AND PNEUMONIC LUNG

(PNEUMOTHORAX-APNEUMATOSIS-PNEUMONIA) *

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Introduction

The Chemistry of Respiration

The Capillary Systems of the Lung

Bronchial system of vessels

Pulmonary system of vessels

Pathologic Physiology

Innervation of the Pulmonary Vessels

Circulation in the Atelectatic (Apneumatic) and Collapsed Lung

Circulation in the Pneumonic Lung

Experimental Data

Technic

Injections of iodized oil

Injections of india ink

Protocols

Injections of iodized oil

Atelectasis of the right lung

Atelectasis of the left lung

Pneumonia of the right middle and lower lobes

Pleurilobar pneumonia

Pneumonia of the right lower lobe

Injections of india ink

Atelectasis of the right lung

Lobar pneumonia

Discussion

Comment

Conclusions

INTRODUCTION

Despite an extensive literature on the circulation in the compressed, collapsed or consolidated lung in pneumothorax, massive atelectasis and lobar pneumonia, we have as yet only few definite ideas on this subject. Views which are most varied, if indeed not diametrically opposed, are

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upheld by different investigators. For the atelectatic lung, opposite theories have been brought forth: (1) an increased blood flow with an impoverishment of blood supply to the healthy lung (Cloetta,¹ Sauerbruch²); (2) a more or less complete suppression of circulation in the affected lung (Weber,³ Brauer,⁴ Bruns,⁵ Propping,⁶ Yates,⁷ Torek,⁸ etc.).

For lobar pneumonia, the same divergence of opinion exists. Lundsgaard and van Slyke,⁹ reviewing different theories relating to the mechanism of the production of cyanosis, said: "We are yet uncertain concerning the main factor in preventing reoxygenation of the blood in the lungs; . . . insufficient oxygenation of blood passing aerated lung tissue or a fraction of blood passing consolidated lung tissue." Stadie¹⁰ found "extensive consolidation without cyanosis, which is against the idea of a shunt . . . that is to say an intact circulation in the unaerated consolidated lung." Ribbert,¹¹ Kline and Winternitz,¹²

1. Cloetta, M.: Ueber die Zirkulation in der Lungen und Beeinflussung durch ueber und unter Druck, Arch. f. exper. Path. u. Pharmacol. **66**:409, 1911. Cloetta, M., and Anderes, E.: Besitzen die Lungen Vasomotoren, *ibid.* **76**:125, 1914. Anderes, E., and Cloetta, M.: Eine weitere Methode zur Prüfung der Lungenzirkulation, Arch. f. exper. Path. u. Pharmacol. **79**:291, 1915; Die Beweis für die Kontraktilität der Lungengefäßen, *ibid.* **79**:301, 1916.

2. Sauerbruch, F.: Zur Pathologie der offenen Pneumothorax, Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1904, vol. 13.

3. Weber, E.: Ueber active Aenderungen der arteriellen Blutfülle der Lungen, Arch. f. Anat. u. Physiol., Suppl., 1914, p. 377; 1912, p. 383.

4. Brauer, L., quoted by Lundsgaard, C., and van Slyke, D.: Cyanosis, Baltimore, Williams & Wilkins Company, 1923, p. 22.

5. Bruns, O.: Ueber die Blutzirkulation in der atelectatischen Lunge, Deutsches Arch. f. klin. Med. **108**:469, 1912.

6. Propping, K.: Ueber den Blutgehalt der Pneumothoraxlunge, Arch. f. klin. Chir. **112**:445, 1919.

7. Yates, J. L.: The Significance of the Vital Capacity in Intrathoracic Surgery, Arch. Surg. **12**:257 (Jan.) 1926; Effects of Acute and Chronic Pneumothorax, Am. J. M. Sc. **1**:165, 1923.

8. Torek, F.: In Discussion of papers on "Acute and Chronic Nontuberculous Bronchopulmonary Suppurative Lesions, Arch. Surg. **16**:316 (Jan.) 1927.

9. Lundsgaard, C., and van Slyke, D.: Cyanosis, Baltimore, Williams & Wilkins Company, 1923, p. 43.

10. Stadie, W. C.: The Oxygen in the Arterial and Venous Blood in Pneumonia and Its Relation to Cyanosis, J. Exper. Med. **30**:215, 1919; The Treatment of Anoxemia in Pneumonia in an Oxygen Chamber, *ibid.* **35**:337, 1922.

11. Ribbert: Ueber die Ursachen der Blutarmuth grau hepatisierter Lungen, Virchows Arch. f. path. Anat. **136**:363, 1894.

12. Kline, B. S., and Winternitz, M. C.: Studies upon Experimental Pneumonia in Rabbits: 8. Intravital Staining in Experimental Pneumonia and the Circulation in the Pneumonic Lung, J. Exper. Med. **21**:304, 1915.

Gross,¹³ Binger and others,¹⁴ on the other hand, tried to show that in pneumonia the circulation is completely cut off in the consolidated lobe. Peabody¹⁵ and Butterfield and Peabody¹⁶ contended that in most cases of uncomplicated pneumonia the decrease in respiratory surface is completely compensated and the oxygen content of the blood is within normal limits; Peabody¹⁷ and Harrop¹⁸ suggested that in rabbits that had received injections of pneumococcus as well as in cases of influenza and influenzal pneumonia in man, the respiratory distress and cyanosis are due to partial conversion of hemoglobin to methemoglobin. But the presence of methemoglobin has never been proved spectroscopically. Lundsgaard and van Slyke⁹ concluded that "the question is of theoretical and practical importance in many respects and needs further investigation."

During our experimental work on massive atelectasis and lobar pneumonia, we were repeatedly faced with this question and decided to investigate it thoroughly. We concentrated chiefly on the circulation in the small branches of the pulmonary artery, and more especially in the capillaries. Injections of different substances were given into the pulmonary circulation in the living animal. The roentgenographic pictures obtained with injection of iodized oil, which showed the condition of the circulation in the branches of the pulmonary arteries and the histologic preparations after intravenous injections of india ink showing the changes occurring in the capillary circulation, demonstrated clearly that none of the foregoing theories is entirely correct. We came to the conclusion that in the three aforementioned pulmonary conditions there is an impairment of the capillary—and only the capillary—circulation; but this is due exclusively to the collapse of the alveoli. The impairment of the circulation follows and is caused by the impairment of the alveolar ventilation. There is no obstruction in the branches of the pulmonary artery and the impairment of the capillary circulation is due neither to the obstruction by emboli nor to compression by intra-alveolar exudate.

13. Gross, L.: The Blood Supply to the Pneumonic Lung, *Canad. M. A. J.* **9**:632, 1919.

14. Binger, C. A. L., and Brow, G. R.: Studies on the Respiratory Mechanism in Lobar Pneumonia, *J. Exper. Med.* **39**:677, 1924. Binger, C. A. L.; Christie, R. V., and Ehrich, W.: Diathermy in Pneumonia, *J. A. M. A.* **91**:367 (Aug. 11) 1928.

15. Peabody, F. W.: The Oxygen Contents of the Blood in Rabbits Infected with *Pneumococcus*, *J. Exper. Med.* **18**:1 (July) 1913; The Oxygen Content of the Blood in Lobar Pneumonia, *ibid.*, p. 7.

16. Butterfield and Peabody, quoted by Austrian, C. R.: Pneumonia in Tice: *System of Medicine*, Hagerstown, Md., W. F. Prior, 1920, vol. 3, p. 1.

17. Peabody (footnote 15, first reference).

18. Harrop, G. A.: The Behavior of the Blood Toward Oxygen in Influenzal Infections, *Bull. Johns Hopkins Hosp.* **30**:10, 1919.

We shall first give a short résumé of a few points in the physiology of the circulation in the lung in relation to respiration, which will be followed by a review and discussion of theories on the circulation in the atelectatic and pneumonic lung. Our experimental observations and our conception of the question, based on them, will then follow.

THE CHEMISTRY OF RESPIRATION

As long as alveolar ventilation and circulation in the pulmonary capillaries are normal, the gas exchange will be normal, and the volumes of oxygen and carbon dioxide will show a remarkable constancy; but if ventilation is impaired by (1) changes in the inspired air, (2) an increase in the thickness of the septums which separate the air sacs from the circulating blood or (3) obstruction of the bronchi or bronchioli, then more or less marked alterations in the partial pressures of oxygen and carbon dioxide in the venous, and particularly the arterial, blood will occur, accompanied by modifications in the p_H of the blood and changes in the urine.

In the case of bronchial obstruction, if the circulation remains intact, an amount of blood will circulate through unaerated channels; it will be overcharged with carbon dioxide, pass through the pulmonary veins into the left side of the heart and pollute the arterial blood. In this way the criterion of persistent circulation in unaerated portions of the lung will be the increase of the partial pressure of carbon dioxide in the arterial blood.

Normally, the partial tension of oxygen in the alveolar air is 107 mm. of mercury, and of carbon dioxide 40 mm. The tensions of the gases in the venous blood in the lung capillaries (Loewy¹⁹) are: oxygen = 5.3 per cent = 37 mm. of mercury; carbon dioxide = 6 per cent = 46 mm. of mercury. There is thus a difference of tension of oxygen between the alveolar air and the blood of $107 - 37 = 70$ mm. of mercury, which will tend to cause a passage of oxygen from the alveolar air to the circulating blood. The total surface of the lung should be, according to Hufner,²⁰ about 140 square meters; even if it has a minimal measurement of 90 square meters, this would be equal to 1,000 square feet. On the other hand, the thickness of the septums separating the capillaries from the alveoli, in which the blood circulates, is a layer no more than one red corpuscle thick, or about 0.004 mm. According to the figures given by Loewy and Zuntz relative to the speed of diffusion of gases, under an alveolar oxygen pressure of only 35 mm. of mercury, 6.7 cc. of oxygen can

19. Loewy, in Starling: *Principles of Human Physiology*, Philadelphia, Lea & Febiger, 1915, p. 907.

20. Hufner, in Starling: *Principles of Human Physiology*, p. 907.

pass through a square centimeter of the alveolar wall in a minute. This amounts to 6,083 cc. of oxygen per minute through the whole surface of the lung, or over 360,000 cc. per hour. The oxygen actually absorbed by a man averages only 350 cc. per kilogram of body weight per hour, or about 20,000 cc. per hour for a person weighing 60 Kg.; this gives an ample margin of safety for increased oxygen consumption; in fact, a difference of pressure of a couple of millimeters would suffice to cause a passage of 300 cc. per kilogram per hour, which is required by the resting man. In the same way it is easy to account for the passage of carbon dioxide in the reverse direction, especially since this gas diffuses twenty-five times as rapidly as oxygen, so that a difference of pressure between the blood and the alveolar air amounting to only 0.3 mm. of mercury would suffice to cause a passage into the alveoli of the 300 cc. of carbon dioxide per kilogram normally expired per hour. We wish to emphasize these figures, which show that in the resting man (or animal) only one-twentieth part of the total surface of the lung is sufficient to insure a normal oxygenation of the blood. A great part of the lung, therefore, could remain unacrated before respiratory disturbance would ensue. This margin of safety, however, is greatly lessened if for any reason the thickness of the septums separating the blood from the alveolar air is increased, as in edema of the alveolar wall, bronchitis (Hoover²¹) or poisoning from gas (Barcroft, Hunt and Dufton²²). Brauer⁴ created the term "pneumonosis" to indicate decreased permeability of alveolar epithelium.

Another important point in the chemistry of respiration is the relation of carbon dioxide tension to the dissociation curve of oxyhemoglobin. With a normal tension of oxygen in the alveolar air (107 mm. of mercury) and of carbon dioxide (40 mm. of mercury), the hemoglobin is 95 per cent saturated. But if the pressure of oxygen falls to 40 mm. of mercury, with a carbon dioxide pressure of 40 mm., the hemoglobin is only about 65 per cent saturated; and at 30 mm. alveolar oxygen pressure it is only 50 per cent saturated (Bohr, Hasselbach and Krogh²³). It has been shown that carbon dioxide acts to split oxygen from oxyhemoglobin, so that as the blood picks up carbon dioxide in its passage through the capillaries, oxygen is liberated from the oxyhemoglobin more readily than would otherwise be possible.

21. Hoover, C. F.: On the Relation Between Blood Flow and Alveolar Ventilation, *J. A. M. A.* **71**:880 (Sept. 14) 1918.

22. Barcroft, J.; Hunt, G. H., and Dufton, D.: The Treatment of Chronic Cases of Gas Poisoning, Great Britain Medical Research Committee, Reports of the Chemical Warfare Medical Committee **4**:13 (April) 1918.

23. Bohr, C.; Hasselbach, K., and Krogh, A.: Ueber einen in biologischer beziehung wichtigen Einfluss, den die Kohlensäurespannung auf dessen sauerstoffbindung übt, *Skandin. Arch. f. Physiol.* **16**:402, 1904.

Moreover, the pressure of salts in the red blood corpuscles greatly influences the dissociation curve of oxyhemoglobin which, in the absence of these salts, takes on the form of a rectangular hyperbola (Barcroft and Roberts²⁴).

In the venous blood, as we have seen, the partial pressure of oxygen is 37 mm. of mercury and of carbon dioxide is 46 mm. The carbon dioxide is combined with the alkalis of the blood. There is a close relation between oxygen and carbon dioxide. Increase of carbon dioxide shifts the dissociation curve of oxyhemoglobin to the right, and a like increase in oxygen helps to liberate carbon dioxide from the blood. As Bohr and Halberstadt,²⁵ Haldane²⁶ and others have shown, more carbon dioxide is given off into the air when oxygen is present. If one lung is ventilated with air and the other with hydrogen, the lung ventilated with air gives off nearly 50 per cent more carbon dioxide than the lung ventilated with hydrogen. Conversely, the blood takes up considerably more carbon dioxide in the absence of oxygen. Oxygenation reduces the carbon dioxide capacity of the blood to such an extent that the partial pressure of carbon dioxide is raised and it can be given off by the blood in the lungs when the carbon dioxide pressure is considerably lower than that of the alveolar air. Thus excessive breathing "washes out" the carbon dioxide of the blood; if such breathing is kept up for a sufficient time it can produce coma and progressive failure in the circulation due to an excessive rise of p_H (alkalosis), as Henderson²⁷ showed. In these cases the available alkali in the blood increases, contrary to acidosis due to excess of carbon dioxide where the available alkali decreases. Henderson and Haggard²⁸ noticed that dangerous symptoms were produced in animals by any considerable increase of the available alkali in the blood when the increase was produced by excessive artificial respiration. Anoxemia, on the contrary, is the condition in which the partial pressure of oxygen in the systemic capillaries is abnormally low. It is due to defective saturation of the arterial hemoglobin with oxygen. Haldane, Meakins and Priestley,²⁹ in experimenting with their "concertina apparatus" by which

24. Barcroft, J., and Roberts, F.: The Dissociation Curve of Hemoglobin, *J. Physiol.* **39**:143, 1909-1910.

25. Bohr and Halberstadt, in Nagel: *Handbuch der Physiologie des Menschen*, 1905, vol. 1, p. 208.

26. Haldane, J. S.: *Respiration*, New Haven, Yale University Press, 1922.

27. Henderson, Yandell: Acapnia and Shock, *Am. J. Physiol.* **21**:126, 1908; **23**:345, 1908-1909; **24**:66, 1909; **25**:310 and 385, 1909-1910.

28. Henderson, Y., and Haggard, H. W.: *Haemato-Respiratory Function*, *J. Biol. Chem.* **39**:163, 1919.

29. Haldane, J. S.; Meakins, J. C., and Priestley, J. G.: The Effects of Shallow Breathing, *J. Physiol.* **43**:3, 1920; **42**:433, 1919.

"shallow breathing" was realized in normal persons, found that when the depth of the respirations was gradually more and more limited the breathing became periodic. Periodic breathing is a characteristic symptom of anoxemia, and it is promptly abolished when a little oxygen is added to the inspired air. According to these authors, the anoxemia is due to unequal and insufficient expansion of the lungs and to the relative increase of the dead space and the uneven ventilation of the alveoli. As a consequence, the venous blood passing through unexpanded parts of the lungs will be imperfectly oxygenated. The amount of oxygen will decrease, although in the expanded portion of the lung hyperventilation prevails and the effect will be a "washing out" of carbon dioxide with an insignificant increase of the oxygen. This is so because the oxygen pressure is only from 16 to 18 per cent of an atmosphere and little oxygen can be taken up by the blood, as is shown by the respective dissociation curves for oxygen and carbon dioxide present in the blood (Haldane³⁰). Another cause of anoxemia is inflammation of the alveoli, which prevents a sufficient volume of oxygen from passing into the blood. This was observed in cases of chlorine poisoning during the war, and is the cause of cyanosis in bronchitis or edema of the lung, etc. The passage of the blood through unaerated channels is another cause of anoxemia, and such a condition obtains in the first stages of atelectasis or pneumonia.

Study of the chemistry of respiration leads to the conclusion that there is an intimate connection between respiration and circulation. Henderson,²⁷ in a series of papers on "Acapnia and Shock," showed that the local circulation in tissues is regulated in accordance with the local carbon dioxide pressure. Haldane,³¹ in his remarkable book on respiration, said: "The main fact must never be lost sight of that the primary factor in determining the rate of circulation is neither the heart nor the venous centers but the metabolic activities of the tissues. At bottom, the regulation of the circulation is a chemical regulation, just as in the case of deep breathing"; this chemical regulation is as accurate and delicate as the regulation of breathing. These conclusions added to the important discovery of Krogh³² of the opening or closing of capillary paths according to local tissue necessities will help us to a better understanding of our subject; for this reason, we feel justified in having dealt at some length with the chemistry of respiration.

30. Haldane (footnote 26, p. 136, fig. 45).

31. Haldane (footnote 26, p. 279).

32. Krogh, A.: *The Supply of Oxygen to the Tissues and the Regulation of the Capillary Circulation*, Am. J. Physiol. **42**:457, 1919; *Anatomy and Physiology of Capillaries*, New Haven, Yale University Press, 1922.

THE CAPILLARY SYSTEMS OF THE LUNG

Precise knowledge of the capillary systems of the lung, pulmonary and bronchial, their interrelations and relative importance and functions, is necessary for a clear understanding of their pathologic processes.

Bronchial System of Vessels.—Miller,³³ in a series of papers, showed that the bronchial artery distributed itself along the entire length of the bronchi, giving small branches which form capillary plexi in the submucosa of the bronchi and bronchioli (as far as the respiratory bronchioli and ducti alveolaris) around the bronchial glands and even in the septums between the alveoli (fig. 1). At almost regular intervals these capillaries join venous radicals which are situated in the mucosa. These venous radicals form a rectangular plexus corresponding to the long axis of the bronchus. From this venous plexus, branches pass through the muscular layer and form a second plexus which is situated along the boundary line between fibrosa and muscularis. The second plexus is the source of venous radicals which, in the deeper part of the lung, form one of the sources of the pulmonary vein; these correspond to the bronchopulmonary veins of Le Fort. On the other hand, the venous radicals which arise from the first two or three divisions of the bronchi do not join the pulmonary vein, but form the true bronchial veins which empty into the azygi, the intercostal veins or the superior vena cava. The important point is that although there are no anastomoses between bronchial arteries and pulmonary arteries, the bronchial capillaries, partly at least, communicate with the pulmonary vein system through the bronchopulmonary veins of Le Fort.

When berlin blue in gelatin under pressure of 112 mm. of mercury is injected into the pulmonary artery, the pulmonary vein being open, the bronchial vessels will not be injected (Miller³⁴). If the injection is made into the pulmonary vein, the pulmonary artery being open, the bronchial vessels will be partially injected. The same will occur if the injection is made into the pulmonary artery, the pulmonary vein being clamped, the berlin blue thus passing retrograde from the capillaries of the pulmonary vein to the bronchial capillary system. But if the injection is made into the pulmonary vein, the pulmonary artery being clamped, there will be a complete injection of the bronchial vessels. This is a clear demonstration of the absence of anastomoses between bronchial arteries and pulmonary arteries; that direct communication between bronchial vessels and the pulmonary venous system exists, is established

33. Miller, W. S.: The Arrangement of the Bronchial Blood Vessels, *Anat. Anz.* 28:432, 1906; The Lobule of the Lung and Its Blood Vessels, *J. Morphol.* 24:459, 1913; *Anat. Anz.*, 1892, vol. 7; Das Lungenlappchen, seine Blut- und Lymphgefäße, *Arch. f. Anat. u. Physiol., Anat. Abt.*, 1920, p. 197.

34. Miller (footnote 33, first reference).

by the following experiment: Miller injected berlin blue in 8 per cent gelatin into the pulmonary vein until it flowed freely from the pulmonary artery. The pulmonary vein was clamped and gelatin containing 8 per cent vermilion granules in suspension was forced into the

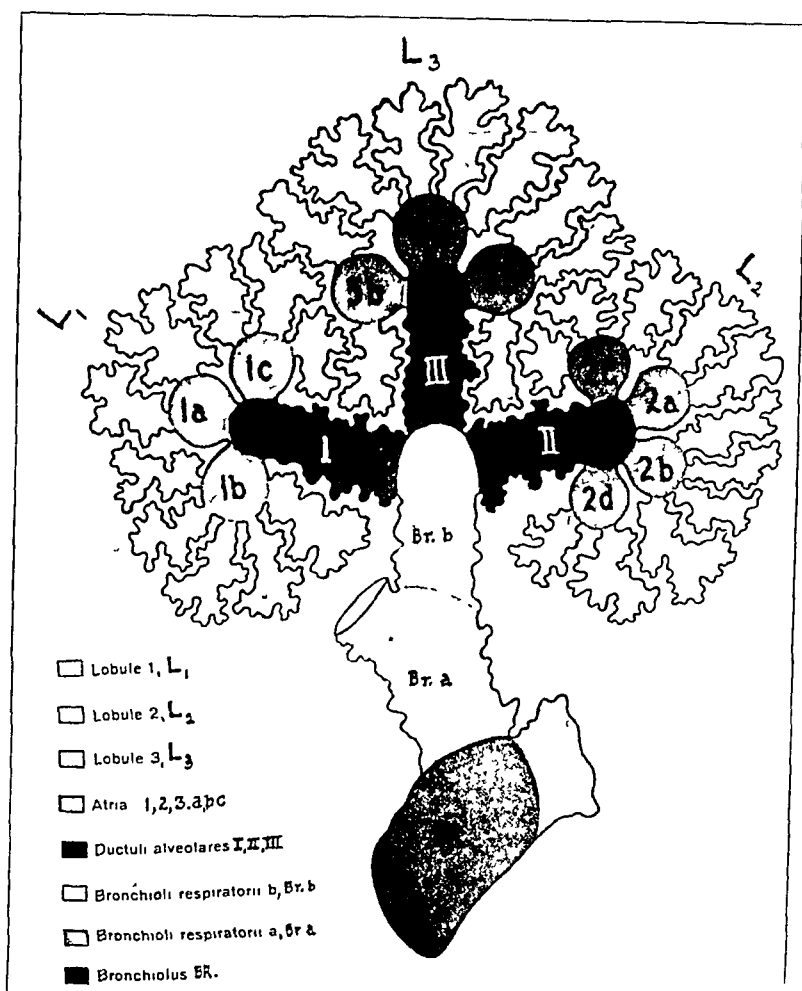


Fig. 1.—Scheme of the air-ways in three lobules of the lungs (after William Snow Miller).

pulmonary artery. The artery showed red, whereas the pulmonary vein and bronchial vessels showed blue. This explains the congestion of the bronchial vessels by a stasis in the pulmonary venous system.

Pulmonary System of Vessels.—The pulmonary capillary system is less complicated than the bronchial. The pulmonary arteries follow the

bronchi and rapidly divide, so that for each bronchus and bronchiolus there is an artery which follows it closely and gives branches to the ducti alveolaris before they are reduced to capillaries around the sacculi. The capillary systems of adjacent alveoli communicate intimately (Sauerbruch³⁵) and are not independent as is so often stated in textbooks. In figure 2 this disposition is clearly shown. These capillaries join venous radicals which unite to form the interlobular veins that extend from the periphery of the alveoli toward the hilum to join a corresponding lobar vein at the proximal region of the bronchioli. Before reaching this point, they receive a part of the blood of the bronchial plexi at the height of the ducti alveolaris and respiratory bronchioli.

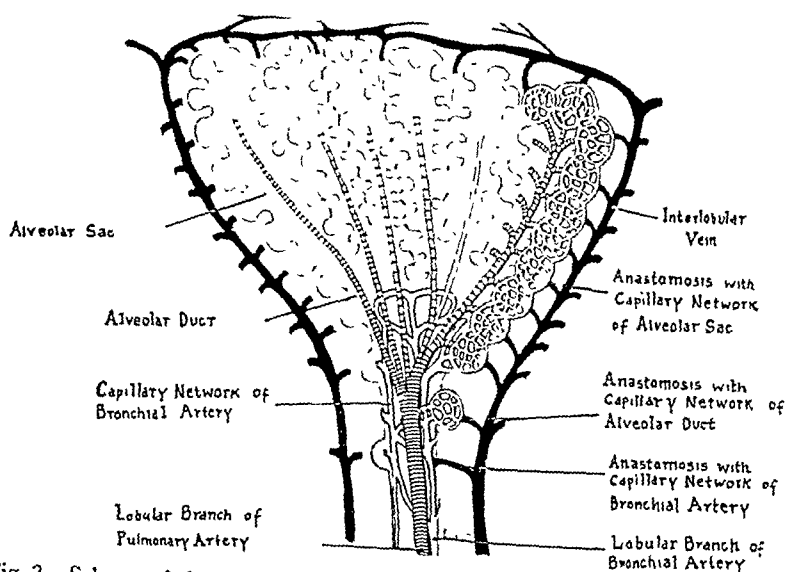


Fig. 2.—Scheme of the blood vessel distribution in the lung (after Sauerbruch).

It is therefore not possible to concede a separation of the two capillary systems, the respiratory (pulmonary artery and vein) and the trophic (bronchial artery and vein). The pulmonary capillaries cover all of the respiratory field of the lung, that is, the alveolar sacs, the atria, the alveolar ducts and the respiratory bronchioli. The bronchial capillary system extends over the bronchi, bronchioli, interalveolar septums and even the respiratory field in order to insure their nutrition. But the bronchial capillaries do not go farther than the ducti alveolaris and the interalveolar septums, so that the nutrition of the alveoli beyond is insured by the pulmonary capillary system. On the other hand, in the walls of the respiratory bronchioli and the ducti alveolaris, there are

35. Sauerbruch, F.: *Die Chirurgie der Brustorgane*, Berlin, Julius Springer, 1920, vol. 1, p. 79

numerous air sacs, so that in these regions the bronchial capillaries function as part of the respiratory system. Hyrtl³⁶ showed that injections through small bronchial arteries always reach the venous alveolar capillaries. Therefore, no sharp distinction between respiratory and nutritive systems can be made in the lung, the pulmonary veins carrying back a part of the blood of the bronchial capillaries. This fact explains why ligation of a branch of the pulmonary artery in animals and in man does not interfere with the nutrition of the alveoli, as Sauerbruch has shown.

Cohnheim and Litten³⁷ did not believe that there was any communication between the two capillary systems. It was Küttner³⁸ who first suggested the wide anastomosis between the two systems, from observation in the frog's lung. Haller,³⁹ Hyrtl,⁴⁰ Henle,⁴¹ Luschka⁴² and Virchow⁴³ maintained that extensive anastomoses exist, and to this view Cohnheim and Litten³⁷ were later converted.

PATHOLOGIC PHYSIOLOGY

The anastomotic disposition of the vascular systems of the lung will regulate the alterations which follow isolated or concomitant ligations or obstructions of one or more of the vessels of the lung—pulmonary artery, pulmonary vein or bronchial vessels.

Ligation of a branch of the pulmonary artery (Bruns,⁵ Sauerbruch,³⁵ Schlaepfer⁴⁴ and Smirnoff⁴⁵) is followed by shrinkage and atelectasis with fibrous sclerosis of the corresponding portion of the lung. These

36. Hyrtl, J.: *Die Corrosions-Anatomie und ihre Ergebnisse*, Vienna, Wilhelm Braumüller, 1873, p. 93.

37. Cohnheim, J., and Litten, M.: *Ueber die Folgen der Embolie der Lungenarterien*, Virchows Arch. f. path. Anat. **65**:99, 1875.

38. Küttner, H.: *Beitrag zu den Kreislaufsverhältnisse der Froschlunge*, Virchows Arch. f. path. Anat. **61**:21, 1874; *Beitrag zur Kenntniss Kreislaufsverhältnisse der Säugethiere Lunge*, *ibid.* **73**:476, 1878.

39. Haller, A.: *Icones Anatomicae. Tabulas Arteriarum Bronchialium*, Göttingen, B. A. Vandenhoeckii, 1756, pt. 8, p. 31.

40. Hyrtl, J.: *Lehrbuch der Anatomie*, ed. 2, Vienna, W. Braumüller, 1851; footnote 36.

41. Henle, F. G. J.: *Handbuch der Eigenweidslehre des Menschen*, Braunschweig, F. Viewig u. Sohn, 1866.

42. Luschka, H.: *Die Anatomie des Menschen*, Tübingen, H. Laupp, 1863, vol. 2, p. 316.

43. Virchow, R.: *Gesammte Abhandlungen zur wissenschaftlichen Medizin*, Frankfurt, Meidinger u. Sohn, 1856, p. 295.

44. Schlaepfer, K.: *The Effect of Ligation of the Pulmonary Artery on One Lung Without and With Resection of the Phrenic Nerve*, Arch. Surg. **13**:623 (Nov.) 1926.

45. Smirnoff, S. A.: *Ueber die Folgen der Unterbindung der Lungenarterien*, Arch. f. klin. Chir. **141**:512, 1926.

alterations are more marked the longer the period of ligation. In nine dogs, Smirnoff ⁴⁵ ligated the pulmonary branch of the lower left lobe. He killed the animals in from ten days to one year and four months. In all cases he noticed "shrinkage of lobe; the lung parenchyma has taken on a solid and airless consistency. Small pieces sink in water. There is a complete physiologic suppression of the lung." None of the aforementioned authors or Küttner,⁴⁶ Kawamura,⁴⁷ Ritter and Ostrowsky ⁴⁸ has ever had a hemorrhagic infarction of the corresponding part of the lung.

Four months after ligation of the pulmonary branch to the left lower lobe, this part of the lung was transformed into "a short solid band."

Sixteen months after ligation, the lobe was extremely small and fleshy, sank in water and had undergone a "fibrous atrophy." Smirnoff ⁴⁵ does not favor the term used by Sauerbruch,³⁵ that is, "carnification," because there is no inflammation with organization of the exudate, but simply an abnormal development of connective tissue especially marked in the perivascular spaces and the interalveolar septums. This connective tissue compresses the alveoli and causes an atrophy of the parenchyma of the lung, but never penetrates the alveoli. Degeneration of the mucosa, atrophy or atypical growth of the bronchial epithelium was noticed, whereas the alveolar epithelium had completely disappeared. The bronchial vessels and their finer tributaries were constantly dilated. It is thus clear that the lesions following ligation of the pulmonary arteries are quite similar to those following ligation of a bronchus. Figure 3 shows the roentgenographic evolution after ligation of the left pulmonary artery. It pictures the striking similarity between the results obtained after suppression of circulation on the one hand and suppression of ventilation on the other, as in cases of obstructive atelectasis. Comparison should be made with our roentgenograms of atelectasis (figs. 10, 12, 14 and 16). The shrinkage of the involved lobes is shown clearly in figures 3 and 4.

Schlaepfer kept dogs with ligated pulmonary arteries for two years. He found the collateral nutritive circulation well established within two months after ligation or within three months in dogs in which he sectioned the phrenic nerve at the same time. The caliber of the bronchial artery is doubled within that period, and from three to four times its normal caliber within two years.

46. Küttner (footnote 38, first reference).

47. Kawamura, K.: Ueber die künstliche Erzeugung von Lungenschrumpfung durch Unterbindung der Pulmonarterienäste, *Deutsche Ztschr. f. Chir.* **125**:373, 1913.

48. Ritter and Ostrowsky, quoted by Smirnoff (footnote 45).

Ligation of the pulmonary vein of a lobe is followed by different results than is ligation of a corresponding artery. As Smirnoff⁴⁹ has shown, the return circulation to the left side of the heart will be completely suspended, so that the blood in the bronchial and pulmonary capillary systems can return only by way of the bronchial veins and so through the azygi, intercostal veins and superior vena cava back again to the right side of the heart. If these collaterals are sufficient, the return circulation might be unimpaired. In the dog these anastomoses are insufficient, and ligation of the pulmonary veins is followed by



Fig. 3.—*A*, normal rabbit's chest. The position of the mediastinum and the heart may be noted. *B*, rabbit chest fifty-seven days after ligation of the left pulmonary artery combined with resection of the phrenic nerve. Silver clips were applied to the nerve. Displacement of the mediastinum and the heart toward the side on which operation was performed may be noted. Cloudiness is seen in lung area on the opposite side. The light area in the lower left side resulted from the displacement of the right mediastinal lobe, interposed between the diaphragm and the left lung. *C*, the same chest after 110 days. Displacement of the mediastinum is more marked. Gradual dilatation of the right mediastinal lobe caused an enlargement of the light area in the lower left region (after Schlaepfer).

49. Smirnoff, S. A.: Versuche uber einfache und kombinierte Unterbindung der Lungengefasse, Arch. f. klin. Chir. **146**:215, 1927

lethal complications, that is, stasis, passive congestion and edema. It is interesting to note what happens in partial occlusion of the pulmonary veins in the dog when survival of the animal is possible. Schlaepfer⁵⁰ ligated the left pulmonary veins in thirteen dogs so as to decrease the diameter to one-fourth the original.

Dogs may die during or shortly after the reduction of the size of the pulmonary vein in from one to two days after operation with increasing dyspnea, congestion, hemorrhages into the lung and dilation of the right ventricle. . . . If the animal survives the acute effect of the operation, complete recovery occurs within forty-eight hours and he remains quite well.

The lung with veins reduced in diameter become smaller than the lung that has not been operated on. A collateral venous circulation is gradually developed in the former through pleuropulmonary adhesions;

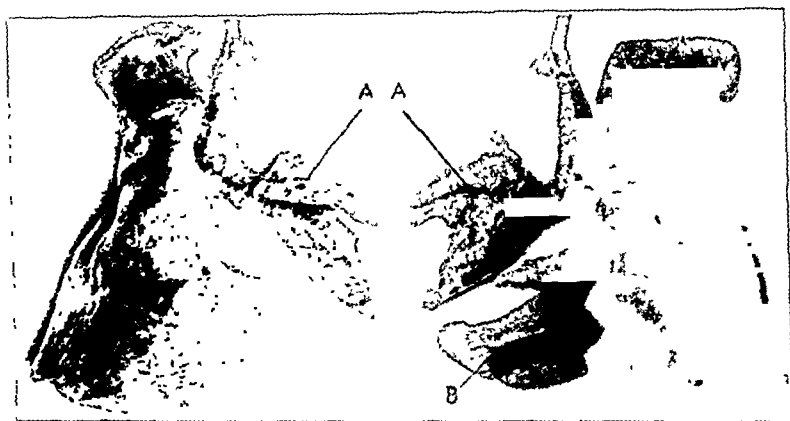


Fig. 4.—Rabbit lung 109 days after ligation of the pulmonary artery combined with phrenicotomy. On the left is the anterior aspect; on the right, the posterior aspect. The small shrunken left lung may be noted. The right mediastinal lobe shows a compensatory dilatation; *A*, shrunken left lung; *B*, right mediastinal lobe (after Schlaepfer).

the bronchial veins are greatly increased in size. Schlaepfer⁵¹ has already shown the clinical importance of this compensatory circulation. The capillaries of the lung that has not been operated on are dilated and

50. Schlaepfer, K.: Morphological Changes Associated with Partial Occlusion of the Pulmonary Veins of One Lung, *Surg. Gynec. Obst.* **42**:679, 1926; Collateral Circulation Following Chronic Obstruction of the Pulmonary Veins and Its Relation to Air Embolus Following Various Diagnostic and Therapeutic Procedures (Pneumolysis), *ibid.* **37**:510, 1923; Fibrosis of the Lung Following Ligation of the Pulmonary Artery: Combined with Phrenicotomy and with Partial Occlusion of the Pulmonary Veins, *Arch. Surg.* **6**:358 (Jan.) 1923.

51. Schlaepfer, K.: Ligation of Pulmonary Artery of One Lung with and without Resection of the Phrenic Nerve, *Arch. Surg.* **9**:25 (July) 1924; footnote 44.

the diameter of the pulmonary artery is greater than on the side on which the operation has been performed. The hemorrhages in the alveoli of the lung that has been operated on gradually disappear, and an irregularly distributed fibrosis is noted.

On the contrary, simultaneous ligation of the pulmonary artery and vein in dogs is well tolerated, the bronchial vessels being able to insure the nutrition of the lung. Smirnoff⁴⁹ concluded that in cases of accidental injury of an important branch of the pulmonary vein in man, necessitating its ligation, it is far better to ligate the corresponding branch of the pulmonary artery as well. In dogs with simultaneous ligation of a lobar pulmonary artery and vein, the lung was found shrunken and airless in from five to seven weeks after operation. Microscopically, there was hypertrophy of connective tissue with atrophy or destruction of the respiratory epithelium as in ligation of the artery alone. The nourishment of the lobe is assured by the bronchial vessels, which through their anastomosis with the pulmonary venous capillaries supply enough blood to the alveoli. There is a "reduced circulation" sufficient, however, to keep the atelectatic and inactive lung alive.

Ligation of bronchial vessels is technically difficult because of their multiplicity of origin and anastomosis with the esophageal, mediastinal, pericardial and intercostal arteries (Bruns and Sauerbruch⁵²). Smirnoff⁴⁹ ligated the bronchial vessels en masse on a bronchus. The animals withstood this operation well. No marked changes resulted in the lung. After thirty-two days the lobe was found to be little decreased in size, was aerated and floated readily in water.

Combined ligation of bronchial vessels and corresponding branches of a pulmonary artery leads to gangrene of the lung. The same result is obtained by combined ligation of bronchial vessels and the corresponding branch of the pulmonary vein.

The foregoing description of the physiology of the circulation of the lung, the relations between the pulmonary and bronchial systems and the absence of necrosis or hemorrhage in cases of occlusion of the pulmonary artery seem in contradiction to the production of hemorrhage which is the outstanding feature described in embolic obstruction of a branch of the pulmonary artery. This discrepancy is only apparent. As pointed out by Karsner and Ash:⁵³ "Hemorrhage is a secondary process . . . it is found but rarely unless some com-

52. Bruns, O., and Sauerbruch, F.: Die künstliche Erzeugung von Lungenschrumpfung durch Unterbindung von Ästen der Pulmonarterie, *Mitt. a. d. Grenzgeb. d. Chir.* **23**:343, 1911.

53. Karsner, H. T., and Ash, J. E.: Studies in Infarction, *J. M. Research* **22**:205, 1927.

plicating condition is present." Grawitz⁵⁴ went so far as to deny the embolic origin of lung infarction, but the work of Fujinami,⁵⁵ Orth⁵⁶ and of Zahn⁵⁷ showed definitely the causative relation between embolism and an infarct. Zahn first drew attention to the fact that passive congestion increased the chances for infarction. Karsner and Ash⁵⁸ came to the conclusion that simple bland embolism of the pulmonary artery produces circulatory changes in the lung area supplied, but not a true infarction, unless there is a previous passive congestion; in the presence of an already existent embolism in the lobe, ligation of the pulmonary vein of that lobe leads to the formation of a true infarct.

INNERVATION OF THE PULMONARY VESSELS

For the sake of completeness, we must consider here the question of innervation of the pulmonary vessels which is at present in an utterly confused state. As Cloetta remarked in 1914,⁵⁸ "Notwithstanding the voluminous literature upon the subject we know nothing about the existence of vasomotors in the vessels of the lung." The recording of pulmonary artery pressures is insufficient to solve the problem because of their wide variations due to the influence of lung movements on the lesser circulation. Tigerstedt⁵⁹ and Krogh⁶⁰ thought that vasoconstrictor fibers existed in the vagus. By electrical irritation of the vagus in a turtle, Krogh⁶¹ observed a decrease in the output from the pulmonary veins on the same side. These observations have not been verified. Later (1922), Krogh⁶² admitted that "this question is still open." Baehr and Pick,⁶³ after much experimental work, concluded that none of the toxic substances that have a bronchoconstrictor or bronchodilator effect on the lung produces even the slightest modification in size of the lung vessels. Weber,³

54. Grawitz, P.: Ueber die hemorrhagischen Infarkte der Lunge, Festschrift der Assisten von R. Virchow, Berlin, 1891.

55. Fujinami, A.: Beitrage zur Entstehung der hemorrhagischen Infarkte der Lunge, Virchows Arch. f. path. Anat. **61**:152, 1898.

56. Orth, J.: Ueber experimentelle Erzeuge der hemorrhagischen Infarkte der Lungen, Verhandl. d. Gesellsch. deutsch. Naturf. u. Aerzte **69**:7, 1897.

57. Zahn, F. W.: Ueber die Folgen des Embolie Verschlusses der Lungenarterien und Pfortaderaste durch Embolie, Verhandl. d. Gesellsch. deutsch. Naturf. u. Aerzte **69**:9, 1898.

58. Cloetta (footnote 1, second reference).

59. Tigerstedt, R.: Ueber den Lungenkreislauf, Skandin. Arch. f. Physiol. **14**:259, 1903.

60. Krogh (footnote 32, first reference).

61. Krogh, A.: The Regulation of the Supply of Blood in the Right Side of the Heart, Skandin. Arch. f. Physiol. **27**:227, 1912.

62. Krogh (footnote 32, second reference).

63. Baehr, G., and Pick, E. P.: Beiträge zur Pharmakologie der Lungengefäße, Arch. f. exper. Path. u. Pharmakol. **74**:65, 1913.

using an oncometer, concluded that vasoconstrictors were present. Cloetta and Anderes⁵⁸ investigated the same subject in cats, rabbits and dogs anesthetized with urethane, paraldehyde, bromdiethylacetamid and ether; in a few cases curare was given. The chest was opened, the common bronchus of the left lung ligated and the right lung placed in the plethysmograph. Oxygen under a constant pressure of 2.5 cm. of water was given through a double tracheal cannula going to the bifurcation of the trachea. The pressures of the pulmonary artery, of the carotid and of the tracing of the plethysmograph, were recorded on the same drum. It is obvious that any slight elevation occurring simultaneously in the curves of the plethysmograph, the pulmonary artery and the carotid would indicate an increase in intrapulmonary blood flow due to increased pressure in the great circulation. This is exactly what happens on intravenous injection of epinephrine, which is without effect on the lung vessels (Cloetta and Anderes⁵⁸).

However, using a substance related to histamine (B. imidazolyethylamine), Cloetta⁵⁸ claimed to have produced strong vasoconstriction of the pulmonary capillaries by the intravenous injection of 1 mg. into the cat; this vasoconstriction is shown by the sudden rise in the pulmonary artery pressure, fall of the plethysmographic curve and an unchanged pressure in the carotid; this would seem to demonstrate the existence of vasoconstrictors. Dale and Laidlaw⁶⁴ agreed with Cloetta;⁵⁸ but Weber,⁶⁵ experimenting with the same substance, noticed vasodilation of the lung vessels, and Baehr and Pick⁶³ observed no effect. Starling⁶⁶ considered that the action of vasomotor nerves is "of little importance and their very existence is questioned by some observers . . . Changes in the calibre of the lung arterioles play under normal conditions, very little part in determining the pressure; on the other hand, considerable changes in the pulmonary pressure are induced by altering the inflow into the right heart and thereby the velocity with which the blood must be propelled through the pulmonary artery and the carotid would indicate an increase in if any, are described as running in the anterior roots of the third, fourth and fifth thoracic nerves. It is generally agreed that no vasomotor nerves of the lung are to be found in the vagi. Fontaine and Herrmann⁶⁷ showed that in the dog, a unilateral section of the first four

64. Dale, H. H., and Laidlaw, P. P.: B-Iminazolyethylamine, Action on the Pulmonary Vessels, *J. Physiol.* **41**:325, 1910-1911.

65. Weber, E.: Entgegnung auf die Abhandlung von M. Cloetta: "Besitzen die Lungen Vasomotoren?" *Arch. f. Anat. u. Physiol., Suppl.*, 1914, p. 532.

66. Starling: *Principles of Human Physiology*, p. 855.

67. Fontaine, R., and Herrmann, L. G.: Experimental Studies on Denervated Lungs, *Arch. Surg.* **16**:1153 (June) 1928.

thoracic sympathetic ganglions, combined with removal of the ansa of Viéussens and the stellate ganglion together with the resection of that portion of the vagosympathetic trunk included in the middle cervical ganglion, does not cause any disturbance in the function of the lung which reacts to all forms of stimulation in the same way as the opposite lung.

We have thus seen that the existence of vasomotor nerves to the lung vessels, either as extrinsic or intrinsic fibers, as well as the problematic question of their physiology, has so far not been proved.

It is evident with how complicated a subject we are dealing, being, as it is, so closely connected with the physiology of circulation in the lung. Under these conditions it is obvious how hazardous it is to assign the pathogenesis of atelectasis to "reflex irritation," "vasomotor reflex" or to "angioneurotic edema" as a number of authors still do. We have insisted on this point in previous papers.

The physiologic and anatomic data already given will render easier the disentanglement of the complicated question of circulation in the atelectatic and pneumonic lung.

CIRCULATION IN THE ATELECTATIC (APNEUMATIC) AND COLLAPSED LUNG

The problem of the relation existing between respiration and blood flow in the lungs is as important as it is complicated. It is important because its exact knowledge will be of great help to the thoracic surgeon who by the mere opening of the thoracic cavity, with consequent collapse of the lung, produces great alterations in the lesser circulation which are still incompletely known factors in the operative results. Fully 75 per cent of the deaths resulting from thoracic operations are due to circulatory troubles. The use of differential pressure (Sauerbruch,² Friedrich and Brauer, quoted by Sauerbruch), artificial pneumothorax, phrenicectomy, thoracoplasty, ligation of branches of the pulmonary artery or even respiration in hypopressure makes knowledge concerning their physiology necessary.

The problem is complicated because other factors besides respiration exert their influence on the lesser circulation, as for example, the pressure on and output from the left side of the heart, the action of the negative intrapleural pressure on the big vessels and the heart, the changes in length of the pulmonary capillaries, the movements of the diaphragm, etc.

Although the controversy started in 1855, there is not as yet to be found in the literature a definite answer to the question whether a collapsed and atelectatic lung contains more blood than the healthy one or even whether the blood flow is greater on expiration or on inspi-

ation We think it advisable to give an historical analysis, as complete as the scope of this work allows, of the previous relevant investigations

Poiseuille⁶⁸ appears to be the first to have experimentally studied the question in his effort to discover the reasons for the production of the successive respiratory movements, that is, inspiration and expiration He studied the capacity of elastic capillary tubes when their length was varied and found that if their length is increased their diameter and their capacity decrease By injecting both collapsed and insufflated lungs with a gelatin mass, he found in microscopic sections that the capillaries were smaller in the insufflated than in the collapsed lobes In perfusing collapsed and insufflated lobes of the same lung, he noticed that a given volume of fluid passed through the collapsed lobes more quickly (3 cc in one minute and twenty seconds) than through the moderately insufflated ones (3 cc in one minute and fifty-nine seconds), in the greatly distended lobes, the 3 cc required two minutes and nineteen seconds for passing through In observing the circulation in the frog's lung under the microscope, he found that the red cells circulated more rapidly when the lung was collapsed than when it was insufflated Donders,⁶⁹ on measuring the intrapulmonary pressures, came to similar conclusions (1858-1859) These two authors believed that on inspiration the capillaries were narrowed and that on expiration they were dilated, according to them, in the collapsed lung this dilatation was even more marked

Quincke and Pfeiffer,⁷⁰ Funke and Latschenberger,⁷¹ Bowditch and Garland,⁷² among the early investigators, accepted Poiseuille's⁶⁸ views On the contrary, Lichthem,⁷³ d'Arsonval,⁷⁴ Zuntz,⁷⁵ de Jager,⁷⁶

68 Poiseuille Recherches sur la respiration, *Compt rend Acad d sc* **4**: 1071, 1855

69 Donders F C Weitere Beitrage zur Physiologie der Respiration und Circulation, *Ztschr f rationelle Med* **4**:241 1853, Beitrage zu Mechanismus der Respiration und Circulation in gesunden und kranken Zustande, *ibid* **3**:289, 1853

70 Quincke and Pfeiffer Ueber den Blutstrom in den Lungen, *Arch f Anat u Physiol*, 1871

71 Funke O, and Latschenberger, J Ueber die Ursachen der respiratorischer Blutdruck-Schwankungen in Aortensystem *Arch f d ges Physiol* **15**:405, 1877

72 Bowditch, H P, and Garland, G M The Effect of the Respiratory Movements on the Pulmonary Circulation, *J Physiol* **2**:91 1879

73 Lichthem, L Die Storungen des Lungen kreislaufs und ihr Einfluss auf den Blutdruck, Berlin, 1876

74 D'Arsonval, A Recherches theoriques et experimentales sur le rôle de l'elasticite du poumons dans les phenomenes de la circulation, These de Paris, 1877

75 Zuntz, N Beitrage zur Kenntniss der Einwirkungen der Atmung auf den Kreislauf, *Arch f d ges Physiol* **17**:374 1878

76 De Jager, S Ueber den Blutstrom in den Lungen, *Arch f d ges Physiol* **20**:426, 1879

Heger⁷⁷ and Heger and Spehl⁷⁸ arrived by different experimental methods at diametrically opposed conclusions; namely, that in the normally inflated lung the capillaries are dilated, that on expiration and in the collapsed lung they are narrowed, and that for these reasons the blood flow in and the blood capacity of the lung are much greater in the expanded lung. Bernstein,⁷⁹ in studying the intrapleural negative pressure in new-born children, found that the negative intrapleural pressure which is absent in stillborn children can easily be produced by the insufflation of the lungs, because the thorax after insufflation of the lungs does not come back to its previous position but remains somewhat expanded. Hermann⁸⁰ explained this phenomenon by the fact that after the insufflation or the first inspirations have overcome the resistance of the alveolar walls which are in contact, the alveoli do not completely collapse again, because at the same time the capillaries of the lung dilate, and the lung which in the fetal state received a very small amount of blood now absorbs the total content of the right ventricle. This change in the pulmonary circulation has as a result the gradual closing off of the two short cuts by which the right side of the heart communicated with the left side and the aorta, namely, the foramen ovale and the ductus arteriovenosus. We shall later return to this important point, the significance of which, we think, has not been sufficiently stressed.

The studies on the disturbances caused by pneumothorax to the circulation and respiration, by Hnatek,⁸¹ Gilbert and Roger,⁸² Arnolds,⁸³ Aron,⁸⁴ Blumenthal,⁸⁵ Kreps,⁸⁶ Lieven⁸⁷ and especially by Sackur,

77. Heger: *Recherches sur la circulation du sang dans les poumons*, Brussels, 1880.

78. Heger and Spehl: *Recherches sur la fistule péricardique*, Arch. de biol., 1881.

79. Bernstein, J.: *Ueber die Entstehung der Aspiration des Brustkorbes bei der Geburt*, Arch. f. d. ges. Physiol. **17**:617, 1878.

80. Hermann, L.: *Ueber den atelectatischen Zustand der Lungen und dessen Aufhören bei Geburt*, Arch. f. d. ges. Physiol. **20**:365, 1879.

81. Hnatek: *Untersuchungen über die Störungen des Blutkreislaufs und der Atmung beim pneumothorax*, Allg. Wien. med. Ztg., 1898, p. 267.

82. Gilbert and Roger: *Etude expérimentale sur le pneumothorax et sur les réflexes d'origine pleurale*, Rev. de méd., no. 233, Nov. 12, 1891, p. 122.

83. Arnolds, A.: *Ein Fall von Pneumotomie wegen Fremdkörper ehe Eiterung eingetreten*, Mitt. a. d. Greng. d. Med. u. Chir. **4**:251, 1899.

84. Aron, E.: *Experimentelle Studien über den Pneumothorax*, Virchows Arch. f. path. Anat. **145**:562, 1896.

85. Blumenthal: *Experimentelle Untersuchungen über den Lungengaswechsel bei den verschiedenen Formen des Pneumothorax*, Ges. Abhandl. a. d. med. Klin. zu Dorpat, Wiesbaden, 1893.

86. Kreps: *Ueber die Atmungsbewegungen bei den verschiedenen formen des Pneumothorax*, Ges. Abhandl. a. d. med. Klin. zu Dorpat, p. 413, 1891.

87. Lieven: *Ueber den Blutdruck bei den verschiedenen Formen des Pneumothorax*, Dorpat, 1893.

gave a new impetus to further experimental and clinical study. Interest was further aroused because of the advances accomplished by the pioneer thoracic surgeons, Quincke,⁸⁸ Garre and Sultan,⁸⁹ Reclus,⁹⁰ Matas,⁹¹ Tuffier and Hallion,⁹² etc.

In 1904, there appeared the epoch-making paper of Sauerbruch,² which marks the beginning of a new phase in the already lengthy discussion of the question. Sauerbruch made a distinction between a lung compressed with, or collapsed without, pneumothorax. He believed that in the lung collapsed without open pneumothorax, where it is in "normal relation with the pleural cavity," the cross-section of the capillary systems is decreased, so that in it "both respiration and circulation are impaired." The lung of the other side undergoes a compensatory distention because "the respiratory increase in the healthy lung, which regularly occurs, is accompanied by an increase in its capillary blood capacity; more blood passes through it, so that notwithstanding the decrease in total respiratory surface, the sound lung can suffice for oxygenation of the blood." He further maintained that in that case there is on inspiration an increase and on expiration a decrease in the blood flow.

But in the collapsed and compressed lung with open pneumothorax, according to Sauerbruch, the circulatory conditions are different. "In unilateral pneumothorax," he said, "more blood passes through the collapsed lung in a unit of time than before establishment of a pneumothorax." He based this conclusion on the experimental observations of Poiseuille,⁶⁸ Quincke and Pfeiffer,⁷⁰ and particularly of Sackur. The latter author, by analysis of the oxygen and carbon dioxide content of the blood from the carotids, before and after pneumothorax, had come to the conclusion that "because of the great dilation of the capillaries of the affected lung, much more blood passes through it than through the sound one, which explains cyanosis and dyspnea." This is in essence the "short circuit" theory.

There seems, however, to be a contradiction here; if collapse of the alveoli produces dilatation of the capillaries, how is it that in the healthy hyperdistended lung there is an increase of blood? As it is of such crucial importance to establish whether Sauerbruch's contentions are correct,

88. Quincke, H. I.: Ueber die Pneumotomie, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **1**:1, 1896.

89. Garre, D., and Sultan, C.: Kritischer Bericht über 20 Lungenoperationen, Beitr. z. klin. Chir. **32**:492, 1901-1902.

90. Reclus, P.: La chirurgie du p^oumon, Rev. de chir. **15**:871, 1895.

91. Matas, R.: The Management of Acute Traumatic Pneumothorax, Ann. Surg. **29**:409, 1899.

92. Tuffier and Hallion: Operation intrathoraciques avec respiration artificielle par insufflation, Compt. rend. Soc. de biol. **48**:951, 1896.

we must dwell on this point yet a while. Sauerbruch claimed the blood flow through the lung was dependent on four fundamental factors: (1) the strength of the right side of the heart, (2) the difference between the pulmonary artery and pulmonary vein pressures, (3) the intrapulmonary pressure and (4) the changes in the diameter of the capillaries following the changes in the volume of the lung. Assuming that the strength of the right side of the heart is constant, with each inspiratory phase there will be an increase in the negative pressure and suction on the thin-walled pulmonary veins and accordingly an increase of the difference in pressures between the pulmonary arteries and veins, as well as a decrease in pressure of the intrapulmonary air; consequently, there will be an expansion of the lung vessels with an increase in their diameter and capacity and an increased blood flow through the lungs. Furthermore, increased negative intrapleural pressure and the suction thus exerted on the big intrathoracic vessels (on the thin-walled veins much more than on the arteries) will have as a direct result an increase in the blood flow from the peripheral veins to the right side of the heart, so that during inspiration the heart will receive more blood in diastole and send more blood in systole than during expiration. Under other conditions, as, for example, on expiration, less blood will come to the right side of the heart and less will leave the left side. Sauerbruch gave the mechanism described and concluded: "The result of these continued causes on inspiration is an increased blood flow in the lungs."

During expiration, several factors contribute to give an opposite effect. These are, according to Sauerbruch, the decrease of the negative intrapleural pressure, the decrease of differential pressure between the pulmonary arteries and the veins, the contraction and decrease in the size of the lung capillaries and, as a result, a decreased flow of blood through the lung.

It is peculiar how, after the foregoing concepts, Sauerbruch² added that "in open pneumothorax an equalization occurs in the pressures exerted inside and outside of the lung, which will have as a result: the further decrease in the difference of pressures between pulmonary arteries and veins, and further that the lung capillaries will be under a steady and unchanging pressure of one atmosphere, and so they will be increased in size in such a way that in open pneumothorax more blood will pass through the collapsed lung than before the establishment of the pneumothorax, and even more than through the sound lung." Such a contention is peculiar, because if, as in expiration, the decrease in difference between intrapulmonary and intrapleural pressures produces a decrease in the flow of the blood through the lung, how can the still further decrease in this difference (in pneumothorax) produce an opposite effect, namely, an increase in the blood flow?

The dyspnea in unilateral pneumothorax would be due, according to Sauerbruch, to the greater part of the blood circulating through the unaerated channels of the collapsed lung and going back to the left side of the heart nonoxygenated. Against Sauerbruch's theory, a great number of arguments can be gathered from his own paper.² On measuring the respiratory air per minute in rabbits before and after unilateral open pneumothorax, he found that after a first period of adjustment in which the number of respiratory movements is increased, the respirations come back to a normal rate with the difference that they become deeper, exactly as after section of one or both vagi. We give here a few of his experimental results (page 413).

1	Rabbit 2,100 Gm	Immediately after Pneumothorax			
1st phase	{	Volume of Air per Minute		Number of Respirations	
		Normal	1. pneumothorax	Normal	1 pneumothorax
		480	530	58	74
2	Rabbit 2,400 Gm	Ten Minutes after Pneumothorax			
2d phase	{	Volume of Air per Minute		Number of Respirations	
		Normal	1 pneumothorax	Normal	1 pneumothorax
		460	470	54	48

The same effects occur if the vagi are sectioned, and Sauerbruch expressed the belief (page 416) that "the stimulation from the lung to the respiratory centre fails in pneumothorax because of the inactivity of the collapsed lung, as also in vagotomy because of the interruption of the nervous connections." We believe it is clear that if the cause of the dyspnea is the increase in carbon dioxide content of the blood, dyspnea should not cease after from two to ten minutes. That dyspnea does disappear would indicate rather that there is no longer an increased carbon dioxide content of blood, which can occur only if the blood is completely diverted from the collapsed lung to the sound one. Another fact against Sauerbruch's views is the remark he made (page 418) that if after the establishment of a mild open pneumothorax one artificially inflates the collapsed lung and clamps the bronchus, the dyspnea ceases immediately. The explanation Sauerbruch gave for this phenomenon is that "all other conditions remaining the same as in open pneumothorax, except the change in volume of the lung, we must admit that the decrease in size is the cause of dyspnea," and "this decrease in size produces the dyspnea by the dilation of the capillaries." We cannot agree with this last statement because in both cases—open pneumothorax with patent or clamped bronchus—the lung is unaerated and the causes of nonoxygenation of the circulating blood are the same (assuming that the blood vessels were

not clamped with the bronchi). We think it is apparent that the absence of dyspnea in the experiment with inflated lung and clamped bronchus is due to the fact that there is no sudden collapse and sudden extra burden thrown on the right side of the heart, as occurs in sudden suppression of the circulation in the collapsed lung. The cause of this temporary dyspnea is to be sought for particularly in the disturbance of the heart.

We do not believe that Sauerbruch is correct in his conception. It would seem that he was forced to it because he considered as definitely proved the conclusions of Poiseuille, Quincke and Pfeiffer, etc., concerning the dilatation of capillaries in the collapsed lung. He was especially influenced by the work of Sackur, who found that in open pneumothorax the arterial blood contained more carbon dioxide and less oxygen than before. It should be mentioned here that Sauerbruch himself later modified (1926) his conception and admitted that his former views were not beyond debate.

In our opinion, the capillaries in the collapsed and atelectatic lung are collapsed proportionately to the shrinkage of the lung with a consequent and proportionate impairment of circulation through the lung.

Cloetta and his collaborators upheld Sackur in his views. Cloetta performed a series of brilliant experiments with the plethysmograph that he invented for the purpose, and came to the following conclusions (1911):

The study of the plethysmographic pulsations of the lung, of the changes of pressure in the carotid, of the pulsations of the right ventricle, of the chemical analysis of the blood and of microscopic sections of inflated and collapsed lung, leads to the conclusion that the hematosis of the lung is better on expiration than on inspiration.

In a more recent paper, Cloetta and Anderes⁵⁸ "determined with the greatest possible accuracy the changes in the lung circulation by recording at the same time plethysmograms of the lung and the pressures in the carotid and pulmonary arteries, in a completely closed gas system." In this paper, Cloetta concluded that "the circulation is incomparably better in the collapsed lung than in the healthy lung."

The opposite point of view is upheld by Bruns.⁵ In a remarkable paper, he exhausted the subject of circulation in the collapsed and atelectatic lung and gave a thorough discussion of the work of Cloetta, whose conclusions he does not accept. Bruns⁵ said:

In the breathing and normally distended lung, the volume and flow of blood are proportionate to the degree of expansion of this organ; . . . In the collapsed lung, the more pronounced the degree of airlessness, the smaller is the blood volume and velocity—and this independently of the cause and mechanism of the collapse (or atelectasis) of the lung.

According to Bruns,⁵ the foregoing conclusions hold for every kind of atelectasis (obstruction of a bronchus, fluid or air in the pleural cavity, or even chronic retraction of the lung). In a general way, he concluded, hematosiis is far better on inspiration than on expiration.

If Poiseuille,⁶⁸ Quincke and Pfeiffer,⁷⁰ and Funke and Latschenberger⁷¹ came to opposite conclusions, this was due to the fact that they used to inflate the lung extracted from the chest with air introduced through the trachea. It is known that the blood pressure in the pulmonary vessels is very low, owing to the small resistance offered by the lung capillaries. According to Sauerbruch,³⁵ it is only from 20 to 30 mm. of mercury, so that in the lung out of the chest, with intrapleural negative pressure removed, it is easy to understand that a combination of atmospheric pressure from without and intrapulmonary insufflation from within can compress the capillaries.

Other experimenters tried to study the capacity of the lung capillaries during inspiratory distention and expiratory deflation by the modifications observed in the systemic blood pressure and the pulse. Unfortunately, a great number of conflicting factors, already enumerated, render the results thus obtained unreliable. Bruns used a direct method in his determinations of the respective blood capacities of the sound and collapsed lungs. He determined colorimetrically the amount of blood contained in the respective lobes and found that the volume of blood in the collapsed lung is regularly smaller, and that this decrease in volume is proportionate to the degree of airlessness of the collapsed lung. Other important points to be determined were: (1) the volume of the blood circulating through the lung vessels during inspiration (with chest intact) but with the heart not subjected to the intrapleural negative pressure; (2) the blood velocity during normal expansion of the lung, with heart and big vessels subjected to the action of the negative intrapleural pressure; (3) the blood velocity in the very expanded lung, the body of the animal being subjected in a closed space to hypopressure (-20 to -30 cm. of water); (4) the velocity of the blood with normal expansion of the lung but under intrapleural hypopressure; (5) the velocity with one lung collapsed, and (6) the velocity with both lungs collapsed.

Bruns answered these questions by skilfully conducted experiments on rabbits. Three-hundredths gram of hirudin was injected by vein, the second, third and fourth ribs were resected close to the sternum and the anterior mediastinum was opened; this can be done in the rabbit without opening the pleural cavities. The heart was displaced out of the chest. A cannula was placed in the trachea and the animal killed by a blow on the neck. Another cannula was rapidly inserted into the origin of the pulmonary artery, and another in the left ventricle, avoiding the entrance of air. The heart was returned to the pericardial

sac again and the animal placed in an airtight box. The three cannulas, tracheal, pulmonary artery and cardiac, were connected to tubes passing through the walls of the box. The cannula of the pulmonary artery was connected with a bottle containing defibrinated rabbit's blood placed 30 cm. above the level of the animal's chest. The results can be summarized as follows: In overdistention of the thorax by extrathoracic hypopressure of -30 cm. of water, neither narrowing of the lung capillaries occurs nor an increase in the blood flow through the lungs. On the contrary, by lowering the intrapulmonary pressure the amount of blood circulating through the lungs is markedly increased. These conclusions are in opposition to Cloetta and Anderes' observations.

Bruns⁵ objected to Cloetta's interpretation of his pulse curves obtained for the lung (collapsed and inflated) enclosed in the plethysmograph. Cloetta⁹³ found that the pulsations of the collapsed lung were much stronger than those of the inflated lung. He explained that by the greater possibility of the blood vessels in the collapsed lung to straighten out from their more or less crooked and tortuous state, whereas in the inflated lung the vessels were already straight and so less apt to have their configuration influenced by the pulse waves. To Cloetta,⁹³ this was an indirect proof that the vessels were elongated in the inflated lung; he concluded that because of this the blood flow through it was decreased. We have previously seen that elongation of the vessels does not necessarily decrease their capacity. Moreover, Bruns⁵ has shown that the height of the pulsations in Cloetta's experiment does not depend on the volume of blood flow, but principally on the concomitant degree of tension within the lung tissue. In order to prove this, Bruns used a special closed glass cylinder containing a thin rubber tube. The pressure within the glass cylinder could be varied, and through the tube a suction and pressure pump sent in with each movement of the plunger exactly the same amount of water; these "pulsations" of the tube were recorded on a kymograph by varying the pressure exerted on the rubber tube from -10 cm. to $+2$ cm. of water. Bruns⁵ obtained a decrease in the magnitude of pulsation on hypopressure, and an increase on hyperpressure. Bruns⁵ thus contended that the magnitude of plethysmographic pulsations is not closely related to or dependent on the blood flow but is proportional to the degree of distention of the lung tissue; and in this conception Tendeloo concurred.

Mathes and his collaborators⁹⁴ found that when water was circulating in a thin rubber tube, the pressure required to compress the

93. Cloetta (footnote 1, first reference).

94. Mathes, M.; Quenstedt; Gottstein, and Dahm: Einige Beobachtungen zur Lehre vom Kreislauf in der Peripherie, *Deutsches Arch. f. klin. Med.* 89:381, 1906-1907.

tube and stop the flow was proportionate to the velocity of the current within it. The conclusion to be drawn from these two experiments is that the magnitude of pulsation of a lung enclosed in a plethysmograph varies according to the internal and external pressures exerted on the walls of the vessels. With inspiratory enlargement of the lung, the volume variations of the vessels and the amplitude of the tracings decrease, whereas the blood flow increases; this is so because of the concomitant dilatation of the vessels and the action of the pulmonary elastic tissue surrounding the vessels, which is stretched on inspiration. To state this in another way, the increased blood velocity, by causing a rise in the pressure exerted on the vessels from within, diminishes their oscillatory capacity. From the size of the pulse wave as recorded in a plethysmograph tracing, no accurate conclusions can be drawn concerning either performance of the heart or volume of the blood flow through the lung. Only the rise or fall of the plethysmographic curve as a whole can give us some information as to the blood volume of the lung. This curve rises on inspiratory inflation of the lung and falls on expiratory collapse, indicating that Cloetta's views are incorrect.

To the impartial observer, Bruns⁵ said it seems altogether inexplicable why precisely at the moment the lung is inflated so as to contain the maximum amount of oxygen the blood flow through the vessels should be reduced to a minimum, and conversely, be increased when the lung contains a minimum of oxygen. What then, would be the reason for supplementary inflation of the lung when the other is collapsed, resected or plugged, and how could the regulation of oxygen and absorption of carbon dioxide remain so constant? The results of Bruns⁵ corroborate the observations of de Jager⁹⁵ and correspond to the figures given by Heger and Spehl,⁷⁸ who found that at the height of inspiration the lungs contain one twelfth of the total volume of blood, whereas at the end of expiration they contain only one eighteenth of the total volume.

Straub,⁹⁶ using the heart-lung preparation of Starling, tried to determine: (1) the relation of the blood pressures at different points of the circulatory system by graphs taken simultaneously of the right auricle, the right ventricle, the pulmonary artery, the left auricle, the left ventricle and the aorta; (2) the volume of blood flowing through a definite cross-section of a vessel in a unit of time; (3) the degree of dilatation of the alveoli, the internal pressure exerted on their inner surface and the pressure on their pleural surface, and (4) the degree of

95. De Jager, S.: *Die Lungencirculation und der arterielle Blutdruck*, Arch. f. d. ges. Physiol. **27**:152, 1881; footnote 76.

96. Straub, H.: *Ueber die kleine Kreislauf. Der Einfluss des grossen Kreislaufs auf das Blutgehalt der Lungen*, Arch. f. klin. Med. **121**:394, 1916.

dilatation of the lung in different phases of respiration. As Straub⁹⁶ remarked, the difficulty of this problem is due principally to the interrelation of the different factors and the changes invoked in the others by modifications of any one of them. Straub's conclusions are of great interest. The volume of blood flowing through the lung depends on the volume of blood expressed by the left ventricle. It depends on the aortic pressure only so far as this can modify the pressure in the left ventricle. Changes in the blood flow to the right side of the heart produce similar changes in the blood flow to the lung, in the pressure within the pulmonary artery and right ventricle. The variations in circulation through the lung produced by changes in the blood flow to the right side of the heart are comparable to those dependent on a variable arterial resistance. In pathologic conditions, however, the former factors play a more important part.

A clear explanation is thus given of the disturbances of the heart found in collapse of the lung, owing to the extra burden thrown on the right chamber because of suppression of circulation over a large pulmonary territory. The same reasoning can account for the hypertrophy maintained for a long time (four months, Bruns⁹⁵). Notwithstanding the slight resistance offered by the lung capillaries and the ease with which they dilate and compensate for functional suppression of relatively large portions of lung (Lichtheim⁷³), there is no doubt that chronic lesions of the lung accompanied by atelectatic alterations are followed by hypertrophy of the right side of the heart (Zuntz,⁷⁵ Gerhard⁹⁷ and Carlstrohm⁹⁸). Weber³ showed the changes in blood volume in the lungs of dogs, cats and monkeys under different conditions. He enclosed a lobe previously ligated (as against a patent bronchus in Cloetta's experiment) in an oncometer and registered at the same time the pressure in the pulmonary artery and aorta. Under these circumstances, the volume changes of the lung must be ascribed to changes in the volume of blood contained. Weber³ distinguished between "passive" alterations in volume which follow closely the arterial pressure and depend on it, and "active" alterations which are independent of arterial pressure. There are two kinds of passive alterations. The first is due to the rise of resistance in the territory of the splanchnic nerves (vasoconstriction of abdominal arterioles) with a resultant increased pressure in the left ventricle and left auricle, and therefore a stasis in the pulmonary vein and a venous stasis in the lung.

97. Gerhard, D.: Beiträge zur Lehre vom Lungenkreislauf und von der mechanischen Wirkung pleuritischen Ergusses, Ztschr. f. klin. Med. 55:195, 1904.
98. Carlstrohm, P. G.: Beiträge zur Frage der Wirkung des künstlichen Pneumothorax auf das Herz und die Zirkulation, Beitr. z. Klin. d. Tuberk. 22: 243, 1912.

The second variety of passive alteration would be due to a rise in the arterial pressure accompanied by increase in venous pressure and increased output of right ventricle.

The active alterations are due to contraction of the lung vessels themselves. Moreover, it is possible that the right side of the heart could increase or decrease its activity independently of the left. It can, for example, contract more vigorously and so produce an active dilatation of blood vessels. In both cases an increase in the content of the blood vessels will follow. It is possible to distinguish one form from the other with certainty, for when the filling of the lung vessels is due to a rise in aortic pressure, the pressure will rise in the pulmonary artery also, whereas in the case of active dilatation of intrapulmonary vessels the pressure in the pulmonary artery will fall. Krogh⁶¹ expressed the belief that there may even be a third form in the passive alteration of the blood volume in the lungs:

By a rise in venous pressure, the output of the right heart will rise also and the blood stream through the lungs will be increased. Such an increase may raise the pressure in the pulmonary artery very slightly, but there can be no doubt that it must raise it and will cause distention of the pulmonary capillaries and veins. Under these circumstances it is absolutely impossible to distinguish between active and passive distension of the pulmonary vessels, except by simultaneous pressure records.

Krogh⁶¹ criticized Weber for failing to record the pressures in the pulmonary artery, and for his assumption that "they present only very slight variations"; he concluded that the large number of volume variations recorded by Weber⁹⁹ as due to nervous stimulation and various drugs does not prove anything.

The possible compression exerted on the capillaries of the lung by intrapulmonary air is discussed by Propping⁶ who remarked that the changes in intrapulmonary pressure when the glottis is open during inspiratory and expiratory phases are very slight, from $+0.1$ mm. of mercury to -0.1 mm. of mercury, according to the figures of Donders.⁶⁹ However,²¹ on forced expiration with the glottis closed after a forced inspiration (Müller's test), or on forcing the inspiration with glottis closed after a forced expiration (Valsalva's test¹⁰⁰), the intrapulmonary pressure may show wide variations; but these variations are of short duration and exert no serious influence on the capillary circulation of the lungs. In discussing the circulation in the consolidated (pneumonic) lung, we will have to deal with this question again.

Among recent authors the consensus is in favor of the view of a decreased circulation in the atelectatic lung. The suppression of the

99. Weber (footnote 3, first reference).

100. Valsalva, A. M.: Opera, Venice, 1740.

circulation in a considerable portion of parenchyma of the lung is rapidly compensated for by the increased circulation in the intact lung. Heuer and Andrus¹⁰¹ showed that after removal of one lung, or even of one lung of one side and one lobe of the other, there occurs, within a few hours, a shifting of the heart, retraction of the chest and elevation of the diaphragm of the corresponding side. The remaining lung fills the thorax completely in from four to six weeks. They followed and measured this enlargement of the remaining lobes under the fluoroscope. The capacity of the lung to dilate is great and indicates the tremendous normal reserve of respiratory surface available. Moreover, within a few hours after operation the animal was not dyspneic. Alveolar air (collected by rebreathing into a bag) and blood specimens were taken immediately; they were taken again in twenty-four hours, in three and five days after operation and thereafter at regular intervals of from several days to one month. The immediate effects were a rise in alveolar carbon dioxide and a fall in oxygen. These alveolar changes were coexistent with a temporary rise in carbon dioxide content of the blood, a marked fall in oxygen, and a rise in oxygen unsaturation. There was a compensatory marked rise in hemoglobin content of the blood and therefore of its oxygen-carrying capacity. These alterations of the alveolar air and blood carbon dioxide and oxygen content were only temporary. They were less marked twenty-four hours after operation and were back to almost normal percentages by the fifteenth day. An important observation was the compensatory increase in hemoglobin (15 per cent), and in the number of red cells (from 1,000,000 to 5,000,000).

In a more recent paper, Andrus¹⁰² stated that collapse of the left lung by ligation of the primary bronchus produces the following immediate results: At first there is a decrease of about 42 per cent in total volume of the lung, this decrease corresponding to that following pneumectomy. The collapsed lung still contains about 30 per cent of the total cardiac output. These two factors cause a 30 per cent reduction in the carbon dioxide of the expired air, an increase in the carbon dioxide content of the arterial and venous blood and a decrease of 5.5 per cent by volume (30 per cent) in arterial oxygen content. To offset these deleterious effects, simultaneous changes of a compensatory nature occur. The respiratory volume per minute and respiratory rate are increased by about 20 per cent. The pulse rate is increased by about 14 per cent with a corresponding increase in the total cardiac

101. Heuer, G. J., and Andrus, W. de W.: The Alveolar and Blood Changes Following Pneumectomy, *Bull. Johns Hopkins Hosp.* **33**:130, 1922.

102. Andrus, W. de W.: Observations on the Cardiorespiratory Physiology Following the Collapse of One Lung by Bronchial Ligation, *Arch. Surg.* **10**:506 (Jan.) 1925.

output, and the circulation through the aerated lung is increased 60 per cent by volume per minute. Lastly, within twenty-four hours there is a marked increase in red cell count and the oxygen-carrying capacity of the blood. The blood carbon dioxide, the carbon dioxide output and the pulse rate, cardiac output and respiratory volume rate per minute return to their preoperative values about fourteen days after operation. The oxygen content of the blood remains below normal for about thirty days, while the volume per minute for the right lung remains permanently elevated. The left lung becomes completely atelectatic within three days after operation—its blood content gradually diminishes to only 8 per cent of the total cardiac output thirty-one days after collapse is established.

Two points from this paper are of particular interest:

(1) The gradual decrease in circulation in the collapsed lung; as it becomes airless the curve of decrease in the circulation through it follows closely the absorption of air for thirty-one hours. The pulmonary blood content falls from 100 to 60 per cent in the first half hour, to 50 per cent by the first hour, to 40 per cent by the fourteenth hour and to 15 per cent by the thirty-first hour. It was 8 per cent by the thirty-first day.

(2) The immediate increase by 60 per cent by volume per minute of the respiratory air. These two facts show clearly the relation between aeration and circulation in the lung, and definitely rule out the view of an increased circulation through the collapsed and atelectatic lung.

It is interesting to note the similarity between the changes following bronchial obstruction and ligation of a branch of the pulmonary artery. In both instances, collapse and then atelectasis of the corresponding lung occur (Bruns and Sauerbruch,⁵² Sauerbruch,³⁵ Kawamura,⁴⁷ Meyer,¹⁰³ Schumacher,¹⁰⁴ Schlaepfer,¹⁰⁵ Scarff¹⁰⁶). Meakins and Davies,¹⁰⁷ in their book on "Respiratory Function in Disease," remarked (page 26) that "if for any reason the air sacs become completely cut off from the inspired air the gases in them will not be renewed and will eventually be completely absorbed, while the blood supply by the pulmonary artery to the collapsed area will become practically nil."

103. Meyer, W.: The Surgery of the Pulmonary Artery, *Ann. Surg.* **32**:189, 1913.

104. Schumacher, E. D.: Die Unterbindung von Pulmonarterienastern zur Erzeugung von Lungenschrumpfung, *Arch. f. klin. Chir.* **95**:536, 1911.

105. Schlaepfer (footnotes 44 and 50).

106. Scarff, J. E.: Pulmonary Blood Pressures, *Arch. Surg.* **12**:591 (Feb.) 1926.

107. Meakins, J. C., and Davies, H. W.: *Respiratory Function in Disease*, Edinburgh, Oliver & Boyd, 1925, p. 26.

Schlaepfer gave¹⁰⁵ a clear demonstration of these facts by detailed experiments on rabbits and dogs. In both, dyspnea follows ligation of a big branch of the pulmonary artery, but this rapidly disappears. This dyspnea, which may or may not be accompanied by cyanosis, is more marked in a mechanical obstruction or ligation of a bronchus (Lichtheim,¹⁰⁶ Coryllos and Birnbaum,¹⁰⁹ etc.); its cause is possibly a reflex transmitted thorough the vagus. The circulatory changes in the lesser circulation are analogous. We quote the figures of Scarff:¹⁰⁶

The increase in the systolic pressure in the main pulmonary artery of a dog after ligation of the left pulmonary artery, varies from 30 to 50 per cent. The pulse pressure varies from 35 to 100 per cent. This increase in both systolic and pulse pressures persists for a number of days but eventually returns to normal. The time required is between seven and twenty-one days, fourteen days being the average time. The adjustment of the pulmonary blood pressure levels after ligation of the left pulmonary artery parallels very closely the physicochemical adjustment in the blood stream.

At autopsy are to be found, besides atelectasis of the corresponding parenchyma of the lung, a "somewhat abnormally thickened right ventricular wall and a difference in the weight ratio between the right and the left ventricle."

Yates¹¹⁰ stressed the close cooperation between the respiratory and circulatory apparatus in maintaining a normal vital capacity:

Deliveries of blood through bronchial arteries and through pulmonary arteries are controlled by the functional activities of the lungs, which are proportionate to vital capacities. . . . When the air cells are inflated the capillaries are elongated and as they carry the air cell walls with them, inflation is increased. These activities and reactions also take place in reverse order.

In order to explain this, Yates¹¹⁰ cited the notion of an air-cell-capillary gear introduced by E. K. Dunham. We agree with Yates on the reversibility of the respiratory-circulatory mechanism. However, we do not very well see the necessity for further complicating the question by a consideration of an air-cell-capillary gear. Decrease in respiratory function of the lung, from whatever cause, produces an oxygen want, an increase in the amount of carbon dioxide in the blood and stimulation of the respiratory center; it increases the amplitude of respiratory movements by throwing into action the accessory respiratory muscles. The inspiratory capacity of the thoracic cavity is increased. This in turn raises the negative intrathoracic pressure and consequently favors the expansion of the alveoli. Under these conditions more blood

¹⁰⁸ Lichtheim, I.: Lungenatektase, *Arch. f. exper. Path. u. Pharmacol.* 10:54, 1879.

¹⁰⁹ Coryllos, P. N., and Birnbaum, G. L.: Obstructive Massive Atelectasis of the Lung, *Arch. Surg.* 16:501 (Feb) 1928.

¹¹⁰ Yates (footnote 7, first reference).

will be brought to the capillaries, because of increased blood flow to the right side of the heart (suction action of increased negative pressure on the big veins), for as de Jager⁹⁵ has shown, a negative pressure acts more readily on the thin-walled pulmonary veins than on the pulmonary artery. Conversely, circulatory disturbances of the lung, from whatever cause (heart disease, hypertension, etc.), will again produce an increase of carbon dioxide, and the phenomena previously cited will be repeated. Furthermore, the production of atelectasis of the lung (without any procedure on the vessels), which limits the respiratory field of the affected portion of the lung, will be followed by a decrease in the amount of blood flow in that portion. Conversely, ligation of the pulmonary artery, without any procedure on the bronchial vessels of the corresponding portion of the lung, will produce a progressive decrease in the respiration and finally complete apneumotosis of the lobe.

In discussing the paper of Yates on "Vital Capacity in Intrathoracic Surgery," Graham mentioned his experiments with Davis¹¹¹ and the work of Chilingworth and Hopkins,¹¹² which are not in agreement with our views. We do not believe that the conclusions of these authors are undebatable. In the experiment of Davis and Graham, "immediately after death from ether the chest was opened and the lower lobe of each lung was removed. One of the principal blood vessels to the lobe was injected with physiological sodium chloride solution. A tight ligature was then placed around the hilum of the lobe including both the vessels and the bronchus, and the lobe was quickly immersed in 10 per cent formalin. In every instance the alveoli of the lobe whose capillaries were distended, were much smaller than those of the other lung." It is obvious that if fluid is injected into the vessels of a collapsed lung there will be produced a dilatation of the capillaries which offer but little resistance, and the capillaries will encroach on the alveolar space. In exactly the same way, with a lung removed from the chest, if the lung is insufflated under similar conditions there is encroachment on the capillaries. It was for this reason that Poiseuille,⁹⁸ Quincke⁹⁸ and Pfeiffer, and Sackur¹¹³ and Sauerbruch² found that the circulation was increased in the atelectatic lung and

111. Davis, H. J., and Graham, E. A.: The Effect of Capillary Distension upon the Size of the Alveoli, to be published; quoted by Lillenthal, H.: *Thoracic Surgery*, Philadelphia, W. B. Saunders Company, 1920, vol. 1, p. 104.

112. Chilingworth, F. P., and Hopkins, R.: Physiologic Changes Produced by Variation in Lung Distension: II. Efficiency of the Pulmonary Circulation in Overcoming Obstruction, *Am. J. Physiol.* **51**:289, 1920.

113. Sackur: Zur Lehre vom Pneumothorax, *Ztschr. f. klin. Med.* **29**:25, 1896; Weiteres zur Lehre vom Pneumothorax, *Virchows Arch. f. path. Anat.* **150**:151, 1897.

decreased in the inflated lung. On the contrary, Underhill¹¹⁴ had noticed a permanent dilatation in the capillaries of the intact lung, and he considered that this is due, partly at least, to the expansion of the alveoli in that lung. Experimentally, von Basch¹¹⁵ showed that a system of rubber tubes wound as a slightly oblique coil about a collapsed rubber bag brought it back to expansion when the tubes were filled with water. When more water was put into the tubes they became further dilated and distended, and the bag expanded more and more; a condition similar to emphysema resulted. These observations obviously are in opposition to those of Davis and Graham.¹¹¹ Furthermore, if their interpretation were correct, then in ligation of the pulmonary artery (without ligation of the vein) expansion and not collapse of the corresponding lung would occur; for if increase in volume of the pulmonary capillaries produces shrinkage of the alveoli, a decrease in their volume should produce distention of the alveoli. Had these authors modified their experiment, this time placing the lung in a closed bell jar under a pressure of from -7 to -10 mm. of mercury, and then injected physiologic solution of sodium chloride under a pressure of $+14$ mm. of mercury, fixation of the lung in formaldehyde certainly would not have revealed an increase in size of the alveoli. With these precautions, approximately normal conditions would have been reproduced. The same reasoning applies to the work of Chilingworth and Hopkins.¹¹²

More recently, Blumgardt and Weiss¹¹⁶ have studied the velocity of blood flow in normal and pathologic conditions by an ingenious method. It consists in injecting into the antecubital vein an active deposit of radium and detecting its arrival in the other arm or in the heart by a modified C. T. R. Wilson closed chamber device. In pulmonary emphysema, where the alveoli are obviously overinflated, and where, according to Davis,¹¹¹ Chilingworth,¹¹² and others, the capillaries should be contracted and blood flow into the lung decreased, Blumgardt and Weiss¹¹⁶ found the opposite to be the case:

Observations recorded demonstrate that even severe chronic pulmonary emphysema does not necessarily obstruct the blood flow sufficiently to interfere with normal velocity of blood flow through the lungs. On the contrary, the velocity is often increased. This increase may be an effort on the part of the

114. Underhill, S. W. F.: *An Investigation into the Circulation Through the Lungs*, Brit. M. J. 2:779 (Nov. 12) 1921.

115. Von Basch: *Klinische und experimentelle Studien aus dem Laboratorium Prof. Von Basch*, Berlin 1:171, 1891.

116. Blumgardt, H., and Weiss, S.: *Studies on the Velocity of the Blood Flow: 1. The Method Utilized*, J. Clin. Investigation 4:1, 1927; *Studies on the Velocity of the Blood Flow in Emphysema*, *ibid.* 4:555, 1927.

circulatory system to compensate for deficient ventilation, in which case it would be another expression of the close interrelation between the cardiovascular and ventilatory systems.

As Bruns⁵ has demonstrated, an extrathoracic hypopressure of 30 cm. of water has no effect on the circulation. He said it is possible (page 482) that a strong negative extrathoracic pressure could stretch some peripheral capillaries beyond the point of elasticity, as Tendeloo¹¹⁷ has shown, and bring about their narrowing. At the same time it would induce an inflation of alveoli which till then were in reserve, and the final result would be an increase in velocity and blood flow in the intrapulmonary circulation. In these experiments, however, one should remember that a strong hypopressure acts not only on the lungs but also on the heart and the systemic veins; this well known action suffices to explain the result obtained by Chilingworth and Hopkins.¹¹² Churchill and Agassiz¹¹⁸ and Churchill¹¹⁹ agreed on the interrelation between respiration and pulmonary circulation:

A portion of lung tissue may expand with an increased volume of both blood and air encroaching upon adjacent areas of the lung, or, with a flexible mediastinum, the volume of an entire lung may become augmented, at the expense of the other side (Churchill and Agassiz¹¹⁸).

It appears, therefore, that the lung by virtue of the altered dynamics of the pulmonary circuit which attends an increased rate of blood flow, is able to increase the effectiveness of its diffusable surface. This mechanism in turn helps to satisfy the increased oxygen demand usually associated with physiological increase in blood flow (Churchill¹¹⁹).

An interesting exposition of this conception is given by Franz Torek:⁸

All matter is subject to certain physical laws and the lung is no exception. If pressure is exerted on any part of the body, for instance on the skin, there will be less blood in it. If suction is applied, the pressure thereby being diminished, the result will be more blood under the area so treated. . . . If the collapsed lung is brought into a negative pressure chamber, so that it will conform to the normal dimensions, there is an exact counterpart of the skin area mentioned before as being under the influence of suction. By thus diminishing the pressure on the outer surface of the lung, a greater amount of blood must infallibly be drawn into the organ. In the normal thorax, this condition of diminished pressure, the negative pressure on the outside of the lung, constantly exists; nature establishes it so that a maximum amount of blood may be sent to the

117. Tendeloo, N. P.: *Lungengedehnung und Lungenemphysemen*, *Ergebn. d. inn. Med. u. Kinderh.* 6:1, 1910.

118. Churchill, E. D., and Agassiz, A.: A Method of Separating the Air Breathed by the Right and Left Lungs Together with the Effect of Pulmonary Circulatory Changes on the Divided Breathing, *Am. J. Physiol.* 76:6, 1926.

119. Churchill, E. D.: The Effect of Increased Blood Flow on the Ratio Between Oxygen Consumption and Pulmonary Ventilation, *Am. J. Physiol.* 86: 274, 1928.

lungs for oxygenation, and with each respiration the suction on the outer surface is increased with a consequent increase in the amount of blood entering the lungs, whereas the expiratory effort drives it out again. . . . We must therefore come to the conclusion that the greatest amount of blood is found in the expanded lung, less in the collapsed lung and least in the compressed lung.

We shall recapitulate this phase of the question with a quotation from Bruns:

The amount of blood in the lung is proportionate to its degree of inflation. The more pronounced is its degree of airlessness the smaller will be the blood volume and velocity of circulating blood. This is true independently of the mechanism of the production of the collapse.

CIRCULATION IN THE PNEUMONIC LUNG

The problem of circulation in the consolidated (pneumonic) lung is still unsolved. There is a characteristic confusion in textbooks and apparent hesitancy on the part of the authors to conciliate these two contradictory facts: the facility with which injections can be made into the vessels and the obvious decrease in the amount of blood that the consolidated lung seems to contain when examined on the autopsy table. There is another cause of confusion; that is, the apparent differences in blood content at different stages of the pneumonic process, as in the stages of engorgement, and red and gray hepatization. "The capillaries of the alveolar walls," according to MacCallum,¹²⁰ "are dilated with blood and there exudes into the air cells fluid from the blood together with leukocytes and red corpuscles." Again, he stated that "the capillaries of the alveolar walls are quite patent, as can be shown by injection, but they seem compressed by the mass of exudate and no longer seem distended with blood." There are no accurate descriptions to be found concerning the state of circulation in the transition stages from the so-called stage of engorgement to that of red or gray hepatization; if the ischemia in the affected lung were due to compression of the capillaries by the exudate, we should expect to find such a graded impairment in the circulation, especially if the consolidation were advancing from the lobuli toward the bronchi as many believe. "In spite of what was said about the state of engorgement, it is rare to find anything but an abrupt transition from a consolidated to an unaffected lung substance" (MacCallum¹²⁰). Some idea may thus be had as to the nicety of our knowledge concerning a fundamental question of pathology.

Lundsgaard and van Slyke,⁹ in their painstaking work on cyanosis, stated: "We are still uncertain concerning the main factor preventing the reoxygenation of the blood." They considered that cyanosis may be

120. MacCallum, W. G.: *A Textbook of Pathology*, Philadelphia, W. B. Saunders Company, 1924.

due to insufficient oxygenation of the blood passing aerated lung tissue (factor designated by these authors by *l*) or to a fraction of blood passing consolidated and unaerated lung tissue (factor designated by *a*). The disappearance of cyanosis after the administration of oxygen (Means and Barach,¹²¹ Barach and Woodwell,¹²² Stadie¹²³), the extensive consolidation found without cyanosis (Stadie¹²³), and the bloodless condition of the consolidated lung in gray hepatization, are, according to Lundsgaard and van Slyke," against the latter hypothesis. "It appears that the blood flow through the affected part is either prevented or much diminished, so that it is not likely to approach the necessary fraction, that is the third of the total blood flow ($a = \frac{1}{3}$), required to cause cyanosis."

Judging the physiologic, anatomic and pathologic evidence available, one inclines to the point of view that the circulation in the pneumonic lung is impaired. Thus far two theories have been proposed to explain this impairment. One attributes it to multiple capillary fibrinous thrombi or emboli in the pulmonary vessels and capillaries; the other, to the compression exerted on the capillaries by the exudate contained in the alveoli. We do not believe that either of these two theories is tenable. Another explanation for the impairment of circulation will be developed subsequently. It is one which is suggested by our experimental observations and seems to be more in conformity with the available data on the lung. Ribbert,¹¹ in 1894, in an addition to an article of Dom Bezzola¹²⁴ on the histology of lobar pneumonia, stated that one should not make inferences from the condition of the lung as seen on the autopsy table, and that it might contain much more blood during life than after death; the color of the blood contained in the capillaries might well be masked by the color of the exudate. There is no doubt in his mind that the pneumonic lung is poorer in blood than the normal one. He rejected the theory of capillary obstruction by compression by the intra-alveolar exudate. The existence in the lumina of the capillaries of fibrinous clots and thrombi was sufficient for him to explain the circulatory deficiency. "In sections colored by Weigert's method in conjunction with carmine, numerous fibrinous deposits were found in the smaller and larger vessels. In some places, a kind of fibrin network with fine threads and large loops were seen; in others, there were more com-

121. Means, J. H., and Barach, A. L.: The Symptomatic Treatment of Pneumonia, *J. A. M. A.* **77**:1217 (Oct. 15) 1921.

122. Barach, A. L., and Woodwell, M. N.: Studies in Oxygen Therapy in Pneumonia and Its Complications, *Arch. Int. Med.* **28**:394 (Oct.) 1921; Studies in Oxygen Therapy with Determination of the Blood Cases, *ibid.* **28**:367 (Oct.) 1921.

123. Stadie (footnote 10, second reference).

124. Dom Bezzola: Beiträge zur Histologie der fibrinöse Pneumonie, *Virchows Arch. f. path. Anat.* **136**:345, 1894.

compact formations always connected with the intima of the vessels. Often real thrombotic processes were encountered as ringlike deposits on the intima, and fibrin and white cells narrowing the lumina of the vessels. There may even be thrombi composed of fibrin, white cells and platelets occluding the vessels more or less completely. Seldom was obstruction observed to be so complete as to permit no passage of blood. Of special interest was the occasional observation of complete thrombosis of all the capillaries around an alveolus without signs of infarction."

MacCallum¹²⁰ is less affirmative as to the cause of anemia. He agrees, however, with Ribbert¹¹ that "one may often find capillaries obstructed by a huge cellular mass which proves to be megalokaryocytes from the bone marrow." Pratt¹²⁵ noticed thrombosis usually only in the smaller vessels and capillaries, consisting of finely granular material seldom completely occluding the lumina of the vessels. Besides, Pratt reported the presence of emboli composed of giant cells from the bone-marrow. He concluded that both the thrombosis and the compression of the capillaries by exudate are more important factors in the anemia and gray color of the consolidated lung than the substitution of white cells for the red which Aufrecht¹²⁶ holds to be the only cause. Aschoff,¹²⁷ Lubarsch¹²⁸ and Maximow¹²⁹ have studied the same giant cells and considered them as causes of embolism in the capillaries and arterioles of the pulmonary arteries. Rindfleisch, on the contrary, considered as the cause of impairment the compression of the capillaries by alveolar exudate. Mallory¹³⁰ is still more affirmative:

As the exudate increases in amount and the fibrin network thickens, the air sacs are greatly distended, the alveolar walls stretched and the capillaries compressed so that they no longer appear engorged. As a result, the redness due to congestion and to some extent to hemorrhage, fades away and the lung passes into the stage known as gray hepatization.

Aschoff¹³¹ attributed the gray color of the consolidated lung to the great number of white cells and to the compression of the capillaries by the exudate.

125. Pratt, J. H.: *The Histology of Acute Lobar Pneumonia*, Johns Hopkins Hosp. Rep. 9:265, 1900.

126. Aufrecht: *Die genuine Lungenentzündung und die bühlshe desquamative Pneumonie*, Deutsche Ztschr. f. Prakt. Med. 45:373, 1875; *Nothnagels spezielle Pathologie und Therapie*, 1899, vol. 14.

127. Aschoff, L.: *Ueber Capillaren embolosus von Nesenkernhaftigen Zellen*, Arch. f. path. Anat. u. Pharmakol. 134:11, 1903.

128. Lubarsch, O.: *Zur Lehre von der Parenchymzellen Embolie*, Fortschr. d. Med. 11:845, 1893.

129. Maximow, A.: *Lehre von der Parenchymzellen-Embolie der Lungenarterie*, Arch. f. path. Anat. 151:297, 1898.

130. Mallory, F. B.: *Principles of Pathological Histology*, Philadelphia, W. B. Saunders Company, 1914, p. 472.

131. Aschoff, L.: *Pathologische Anatomie*, ed. 6, Jena, G. Fischer, vol. 2, p. 284.

The latter opinion is upheld by Christie, Ehrich and Binger,¹³² who, in experimental studies on diathermy in pneumonia, observed an elevation of temperature in the pneumonic lung in the dog. They found in pneumococcus type I and *B. friedlander* experimental pneumonia that in most instances a more rapid rate of heating occurred in the affected than in the normal lobes. This local heating was of the order and magnitude found in a lung of which the branch of the pulmonary artery supplying it had been clamped. The authors injected barium gelatin mixture into the pulmonary arteries (in lungs of a pneumonic dog) and they found that there was an obstruction of the pulmonary artery branch in the area corresponding to the part of the lung which showed gross pathologic changes at autopsy. They do not, however, consider this specimen as definite proof of vascular obstruction, and are rather inclined to believe that there was a faulty technic (personal communication). In man, the results were not so marked as for the dog. They concluded that there is a marked impairment in the circulation in the pneumonic lobes but that this is due to compression of the capillaries by the alveolar exudate.

Gross¹³ injected oxychloride of bismuth in gelatin into pneumonic lungs, post mortem. In the healthy lung the vessels are uniformly injected (fig. 5). He concluded in his work that varying degrees of vascular obliteration may occur depending on the stage of the consolidation. In red hepatization there is a moderate impairment of the circulation and although the involved parenchyma of the lung, macroscopically at least, looked as though nonfunctioning, there was still a moderate circulation going on. On the contrary, in gray hepatization there is a complete lack of injection and only large branches, ending abruptly, are injected; the whole area of gray hepatization shows a strikingly anemic condition (fig. 6).

The most complete experimental study on this question was made by Kline and Winternitz.¹² These authors observed that when pneumonia is produced in animals which were previously given injections of vital stain (trypan blue), the involved lung had a uniform blue color. However, when the dye is injected from twenty to sixty-five hours after pneumonia is produced, the normal lung will appear a uniform blue whereas the consolidated areas will not take the dye. These areas present a pale gray color, as do the nonstained specimens. The sharp demarcation of these wedge-shaped infarct-like areas was so striking that these authors investigated the question further. In a

132. Christie, R. V.; Ehrich, W., and Binger, C. A. L.: An Experimental Study of Diathermy: 5. The Elevation of Temperature in the Pneumonic Lung, *J. Exper. Med.* **37**:741 (May 1) 1928. Binger, Christie and Ehrich (footnote 14, second reference).

case of pneumonia of the right middle and lower lobes in man, three and one-half hours after death, they injected into the pulmonary artery equal parts of 5 per cent berlin blue in 10 per cent gelatin under a pressure of 120 mm. of mercury. After the injection, the pulmonary artery was tied and the lungs placed in a diluted solution of formalde-

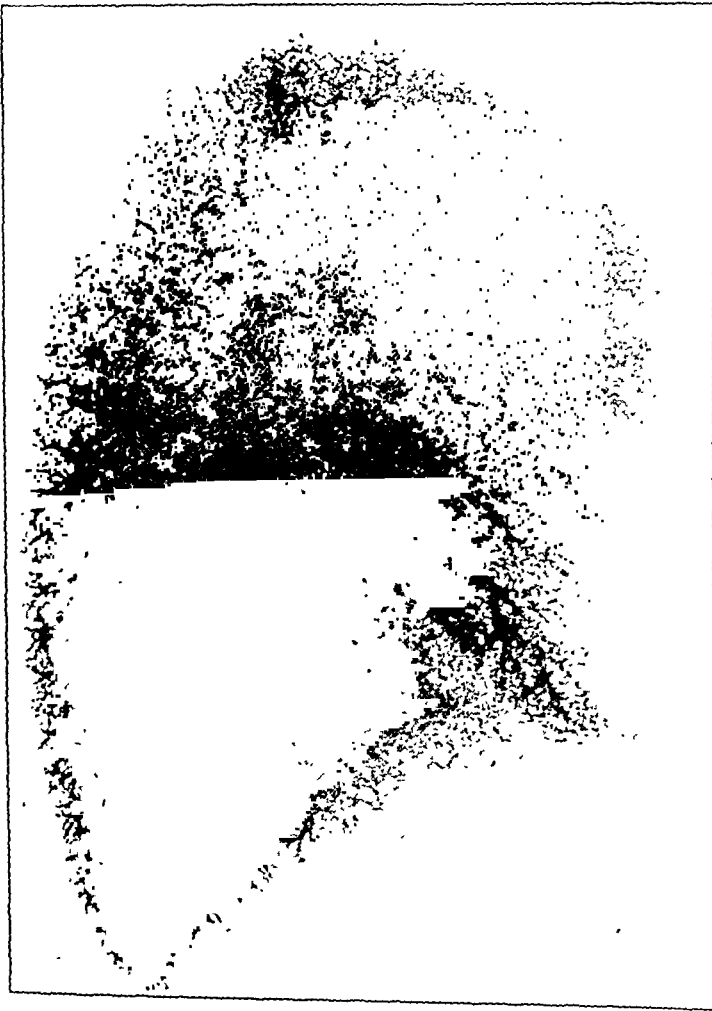


Fig. 5.—Normal lung into which bismuth oxychloride gelatin was injected through the pulmonary artery (after Gross).

hyde, U. S. P. (1:10) overnight. The following morning a striking picture presented itself. The consolidated area was pale gray, whereas the healthy lung was intensely blue. Four subsequent specimens treated in the same way yielded similar results. The same results were obtained with injections into pneumonic lungs of rabbits after death. Micro-

scopic sections in man and in rabbits showed that little blue solution had penetrated the consolidated area, whereas the vessels of the healthy lung were engorged with the blue solution. Apparently there was an impairment of the circulation in the consolidated lung, at least in the postmortem specimen.



Fig. 6.—Roentgenogram of a lung from a case of lobar pneumonia into which bismuth oxychloride-gelatin was injected. *A*, consolidated area—gray hepatization—the main vessels though constricted are functioning while the finer vasculature has been obliterated. *B*, consolidated area—red hepatization—the main vessels are constricted and the finer vasculature is less dense than normal. *C*, healthy lung tissue except for compensatory congestion. The main and finer vasculature is conspicuously dilated (after Gross, with whose results we are not in agreement).

As a cause of such impairment, the authors considered the following hypotheses: (1) compression of the alveoli by the intra-alveolar

exudate and (2) obstruction of the blood vessels by fibrinous thrombi. Into the rabbit's lung, the left lobe of which was distended with air so that its volume was considerably greater than if it had been the site of lobar pneumonia, they injected the gelatin berlin blue mass into the pulmonary artery under a pressure of 120 mm. of mercury. The result was negative. Macroscopically and microscopically, there was no difference in color between the distended and normal lobes.

In another set of experiments they injected a 10 per cent gelatin solution at body temperature into the left bronchus under a pressure of 120 mm. of mercury. The lungs were then placed in cold water to allow the gelatin mass to solidify, after which a gelatin berlin blue mass was injected through the pulmonary artery. Both macroscopically and microscopically, the distended as well as the deflated areas were colored uniformly blue; there were no differences in penetration of dye in the capillary vessels. In other rabbits, freshly drawn rabbit blood was injected into the bronchus of one lobe to distend the alveoli, and then the same gelatin blue solution was injected into the pulmonary artery. Again negative results were obtained. These experiments indicated that the impaired circulation in the pneumonic lung cannot be due to the pressure of exudate within the alveoli. The only remaining factors to which the pallor and impairment of circulation could be ascribed by Kline and Winternitz¹² were the white cells, the fibrin or both. Aplastic anemia was therefore produced in rabbits by injections of benzene until the white cell count was under 1,000 per cubic centimeter, and then pneumonia was produced. Twenty-four hours later, A berlin blue gelatin mass was injected into the pulmonary artery. No coloration of the consolidated lungs occurred, whereas the normal lungs were deep blue. In microscopic sections, the interesting observation was made that the exudate contained few leukocytes and consisted almost entirely of fibrin. This is an additional proof that the gray coloration cannot be due to the white cells alone; nor can the impairment of the circulation be ascribed to compression by the exudate due to the influx of white cells into the alveoli during the phase of gray consolidation.

In order to determine whether the fibrin was the principal factor in vascular obstruction, Kline and Winternitz produced pneumonia in animals in which fibrin formation was inhibited by the use of a solution containing phosphorus in olive oil and 0.9 per cent chloroform in 30 per cent alcohol. This was given by stomach on two successive days. Twenty-four hours later the clotting time of the blood was found to be greatly delayed, and the resulting clot soft and jelly-like. Pneumonia was produced by intratracheal insufflation of pneumococcus. One animal died seventeen and one-half hours later. At autopsy, it showed "con-

solidation of practically the entire left lobe. . . . Berlin blue gelatine was then injected into the pulmonary artery. On sections the consolidated lung was found to be almost as uniformly blue as the uninvolved lobes. Microscopic sections showed that the exudate contained an abundance of cells but very little fibrin. Furthermore, the vessels in consolidated area, contained a much greater amount of dye than had been observed in any of the other pneumonic lungs."

It is seen from the foregoing observations that most workers are inclined to the view that the circulation in the pneumonic lung is impaired. This fact is perhaps much more important than it has heretofore been considered. As Kline and Winternitz pointed out, it might help one to understand the inefficacy of serum or other therapeutic methods in lobar pneumonia after the third or fourth day of the disease. Moreover, it could explain the crisis or lysis in this disease which so uniformly occurs between the fifth and eleventh day. According to this conception, therapeutic substances introduced by mouth, hypodermically or by vein cannot reach the affected lung (the focus of infection) because of the circulatory impairment. The crisis could be explained on the same basis, for little serum can reach the consolidated area at this stage; so that the proteolytic ferments liberated by the white cells (Opie¹³³ and Lord¹³⁴) are not neutralized by the antitryptic power of the serum; the digestion of fibrin in the exudate thus proceeds unhampered.

The mechanism of circulatory impairment requires a much more detailed investigation. Kline and Winternitz¹² ruled out the theory of compression of lung vessels by exudate. This opinion of Kline and Winternitz is in accord with our own view: the pneumonic lung being smaller than the healthy one, as we have previously shown,¹³⁵ renders the acceptance of the compression theory difficult. Concerning the view of thrombosis and embolism of the capillaries as factors in impairment, we shall simply state that it is not in agreement with our knowledge about pulmonary infarction and the lesions produced by it. There is no apparent reason for the strict localization of this thrombotic or

133. Opie, E. L.: Intracellular Digestion: The Enzymes and Anti-Enzymes, *Physiol. Rev.* **2**:252 (Oct.) 1922; The Enzymes in Phagocytic Cells of Inflammatory Exudates, *J. Exper. Med.* **3**:410 (May) 1926.

134. Lord, F. T.: The Relation of Proteolytic Enzymes in the Pneumonic Lung to Hydrogen Ion Concentration: An Explanation of Resolution, *J. Exper. Med.* **30**:379, 1919; Pneumonia, *Harvard Health Talks*, 1929, no. 9, Cambridge, Harvard University Press. Lord, F. T., and Nye, R. N.: Studies in Pneumonic Exudate, *J. Exper. Med.* **34**:201, 1921.

135. Coryllos, P. N., and Birnbaum, G. L.: Lobar Pneumonia Considered as a Pneumococcic Massive Atelectasis of the Lung, *Bull. N. Y. Acad. Med.* **4**:384, 1928; Lobar Pneumonia, *Arch. Surg.* **18**:190 (Jan.) 1929; The Size of the Consolidated Lung in Lobar Pneumonia, *Am. J. M. Sc.* **178**:15 (July) 1929.

embolic process to the small branches and capillaries of the pulmonary artery alone, while the bronchial arteries and peribronchial capillaries, on the other hand, remain unaffected. For reasons developed in an earlier part of this paper, we should expect infarction and trophic disturbances of the parenchyma of the lung if thrombosis of both systems of vessels were present. Finally, we wish to add that the results obtained by injection into the pulmonary artery both by Binger and his collaborators,¹³⁶ Gross,¹³ etc., of such substances as these authors used, are open to serious objections, especially since postmortem specimens were used.

EXPERIMENTAL DATA

The desideratum in an injecting substance is that (1) it should be nontoxic and injected into the right side of the heart of the living animal; it must produce no alterations in the blood (like coagulation of the albumin); (2) it should be fluid enough to pass through the smallest ramifications of the pulmonary arteries, and (3) have radiopaque properties for its detection in roentgenograms. Thus far the substances used by Gross¹³ (oxychloride of bismuth in gelatin) or by Binger and others (powdered barium sulphate in gelatin) or the vital stains of Kline and Winternitz¹² fall short of these requirements.

For these reasons, we used iodized oil 40 per cent. The results were surprising and quite different from those of other investigators. Iodized oil proved to be the ideal substance for this purpose because it can be injected into the jugular vein of the living dog without pressure and in amounts (from 10 to 40 cc.) compatible with survival of the animal for several minutes. Ample time was thus given the right side of the heart to propel the substance through the pulmonary artery to the lungs of its own accord. Roentgenograms showed that there was no obstruction in the vascular tree of the pulmonary artery, a condition which Gross,¹³ Binger¹³⁷ and co-workers, and Kline and Winternitz¹² believed to exist and figured (figs. 5 and 6). The smallest ramifications of the pulmonary artery were clearly shown in fine detail in the diseased portions of the lung as well as in the healthy lung. From roentgenograms of the lung alone the affected lobes cannot be distinguished from the healthy lungs.

The patency of the pulmonary arterial tree was thus established. However, this gave us no information about the more important question of circulation in the capillaries of the lung. The fact that the finest arborizations of the pulmonary artery were so clearly shown

136. Branch, A.; Brow, C. R., and Binger, C. A. L.: *Internat. Assoc. Med. Mus. Bull.*, 1925, no. 10, p. 48.

137. Binger; Christie and Ehrich (footnote 14, second reference). Branch; Brow and Binger (footnote 136). Christie; Ehrich and Binger (footnote 132).

raised doubt in our minds about the ability of iodized oil to pass through the precapillary arterioles. Roentgenograms of the heart, after the aorta was clamped, showed the right side of the heart still filled with iodized oil, but no trace of it was discernible in the left side (fig. 7). This showed us that iodized oil was not a suitable substance for investigation of the capillary circulation.

For that purpose we used the technic first suggested by Krogh⁶² and later used by Binger, Brow and Branch¹³⁶ in their study of their



Fig. 7.—Heart after injection of iodized oil into the jugular vein. The right side of the heart is filled with oil, but there are no traces of it in the left side, showing that iodized oil does not pass through the pulmonary capillaries back to the left side of the heart in this short time.

“starch” lungs. A 20 per cent solution of india ink in Ringer’s solution is injected through the jugular vein of the living animal after the blood is washed out with a stream of Ringer’s solution heated to body temperature. Perfect injection of the capillaries can be obtained. In microscopic sections of the normal lung, the capillaries are black and outline the alveoli clearly. By this method we were able to visualize the changes in alveolar size both in experimental atelectasis and in pneumonia, and the changes in the shape, size and content of the capillaries

incident thereto. The similarity of changes in the circulation revealed for both diseases is really very striking.

For a detailed description of the technic of experimental production of atelectasis and pneumonia, we refer the reader to previous papers.¹³⁸

TECHNIC

Injections of Iodized Oil.—Thirty-four dogs were used, sixteen with atelectasis and eighteen with pneumonia. Atelectasis was produced from twenty-four to forty-eight hours previously by our method. Pneumonia was induced from six to thirty-six hours previously by the intrabronchial insufflation of pneumococcus type 1, by our technic.

The animals were anesthetized with a 10 per cent solution of iso-amyl-ethyl barbituric acid, given intraperitoneally in a dosage of 55 mg. per kilogram of body weight. The right external jugular vein was prepared, a cannula introduced, the distal part clamped with a serrefine and the animal placed on our x-ray stand. The iodized oil was warmed to body temperature and injected into the vein in amounts of 10 cc. This quantity was injected in one minute; very little pressure on the piston of the syringe was necessary. Serial roentgenograms were taken at intervals of from one to five minutes. The animals showed a variable ability to withstand the injections of iodized oil; they generally survived the injection of 10 cc. for from ten to forty minutes, or even sixty minutes. The atelectatic animals were far more resistant than the more toxic pneumonic dogs.

Forty cubic centimeters of iodized oil is uniformly fatal, the animals surviving only from two to five minutes. Smaller doses of 5 cc. may be withstood for twenty-four hours and doses of 1 or 2 cc. do not appreciably affect the animal. This point is now under investigation.

Injections of India Ink.—Atelectatic and pneumonic dogs were used; the usual anesthesia was given. The external jugular vein was dissected free and sectioned between two serrefines. Cannulas were introduced into both the distal and the proximal cut ends of the vein. Injections were made with the simple aid of gravity; that is, the levels of the injecting fluids were 50 cm. above the level of the heart. Ringer's solution and a 20 per cent solution of india ink in Ringer's solution, 1,500 cc. of each, at body temperature, were placed in 4 liter bottles which were held bottom side up on a special rack. These bottles were so connected by rubber tubing to a glass "Y" tube that one or the other solution could be let into the vein. When it was time to begin the injections, the blood was allowed to flow out of the upper cut end of the jugular vein, while at the same time Ringer's solution was introduced into the proximal cut end. In this way the blood was being continuously washed out of the circulatory system, and when the return flow from the cephalad cut end of the jugular vein was of a thin, watery consistency, the injection of Ringer's solution was stopped and immediately replaced with an injection of india ink. Generally, within from ten to fourteen seconds, the india ink would appear at the upper (cephalad) cut end of the jugular vein. It is well not to push the washing out with Ringer's solution too far before shifting to the india ink for the animal rarely survives for more than two or three minutes after the injection of ink is started. Usually from 1,000 to 1,500 cc. of Ringer's solution is sufficient for the technic described.

After the death of the animal, the trachea was clamped to avoid collapse of the lung. When the chest was opened, the lungs were found to be uniformly

138. Coryllos and Birnbaum (footnotes 109 and 135).

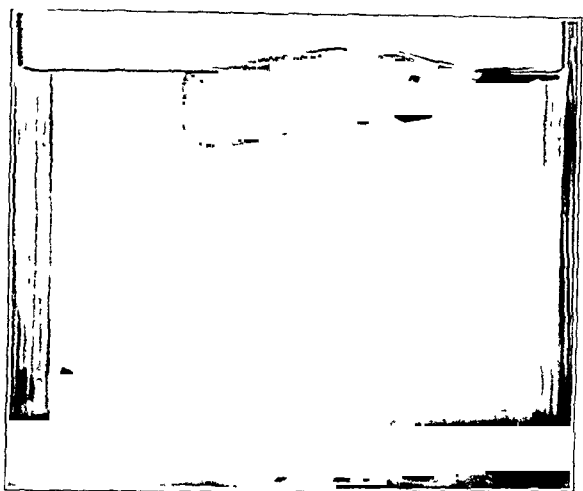


Fig. 8.—Hydrostatic test of degree of airlessness. The normal lung floats; the completely apneumatic lung sinks readily in water.

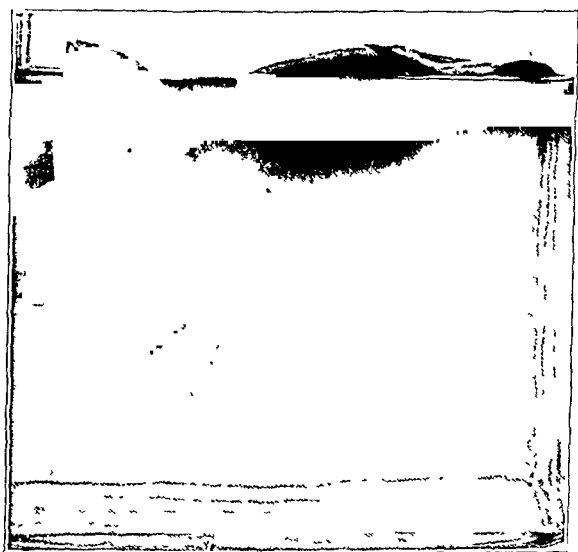


Fig. 9.—Hydrostatic test of degree of airlessness. The left lung is aerated and floats. The right lung shows varying degrees of airlessness. Small specimens from the upper part floated; those from the midportion submerged, and those from the lower part slowly sank in water.

black. In some cases there were patches of less deeply colored tissue, but these were met with in healthy portions of the lung as well as in the affected lung. They were due, we believe, possibly to incomplete washing out of the blood. After the death of the animal and before the lungs were removed from the chest, all main vessels to and from the heart and to and from the lungs were carefully ligated. Small specimens about 1 cc. in size were cut from different portions of the lung to test their degree of atelectasis when allowed to fall into a container of water. We distinguished four groups: floating, submerging, slowly sinking and readily sinking. We have always found the degree of atelectasis as shown by microscopic section proportionate to the readiness with which the specimen of lung sinks to the bottom in a container with water (figs. 8 and 9).

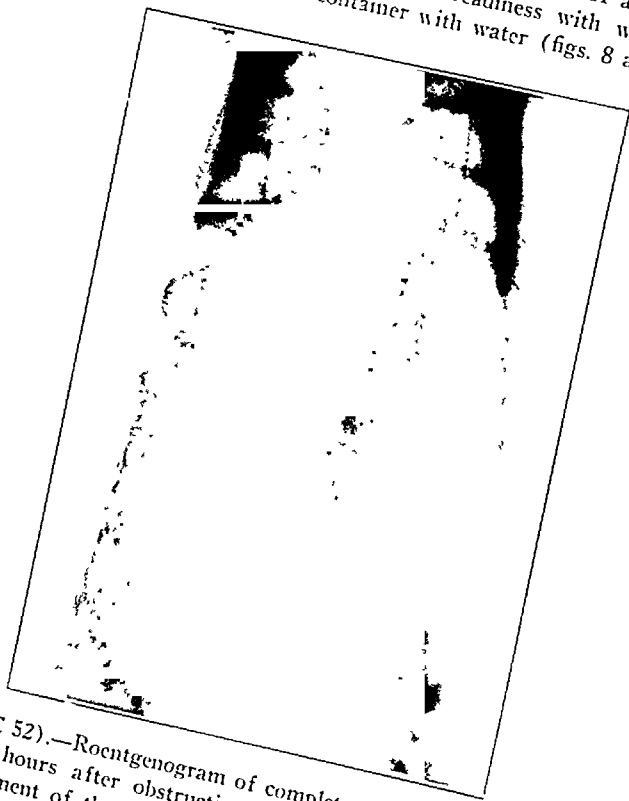


Fig. 10 (dog C 52).—Roentgenogram of complete atelectasis of the right lower lobe twenty-four hours after obstruction of the right lower lobe with special balloon. Displacement of the heart to the right and elevation of the right side of the diaphragm are plainly seen. The balloon is outlined.

Specimens were fixed in a diluted solution of formaldehyde, U. S. P. (1:10) for microscopic section. Both stained and unstained sections were prepared.

PROTOCOLS

We shall give only seven protocols, each representative of its group: five for injections of iodized oil (atelectasis of the right and left lungs, pneumonia of the right and left lungs and pleurilobar pneumonia), and two for injections of india ink (one in atelectasis and one in pneumonia).

INJECTIONS OF IODIZED OIL

I. Atelectasis of the Right Lung: Dog C 52 was used in this experiment.

March 20, 1928, 10:00 a. m.: The right lower lobe was blocked with our balloon.

March 21, 10:00 a. m.: Roentgen examination showed atelectasis of the right lower lobe (fig. 10). Displacement of the heart and trachea to the right and elevation of the right side of the diaphragm were plainly seen. Iso-amyl-ethyl barbituric acid anesthesia was used.

11:00 a. m.: Ten cubic centimeters of warm iodized oil was injected over a period of one minute into the jugular vein. Roentgenograms were taken every three minutes. After the injections, the dog developed dyspnea and shallow

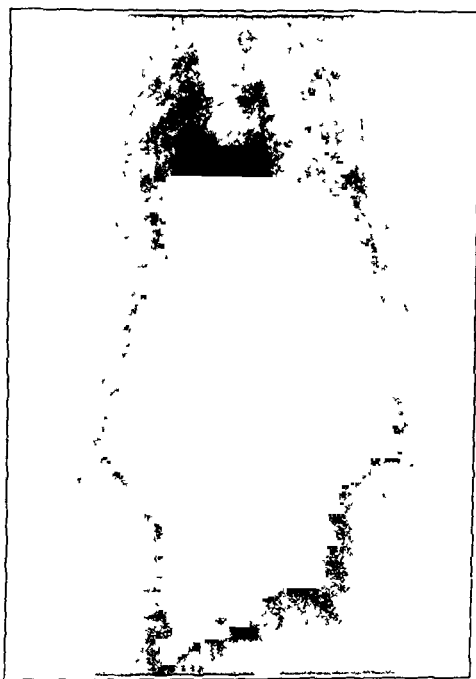


Fig. 11 (dog C 52).—Roentgenogram taken just before death of the animal showing the pulmonary artery injected with iodized oil; the branch to the involved right lower lobe is markedly dilated.

breathing which lasted for about two minutes; 10 cc. more of iodized oil was injected. The animal again became dyspneic, and forty-five minutes later the heart action became weak; the heart stopped shortly thereafter. Figure 11, taken before the death of the animal, shows both pulmonary arteries injected, but the branch corresponding to the involved right lower lobe is dilated.

At postmortem examination, the trachea was clamped, the lungs extracted and the large vessels of the heart and of the hilum of the lung clamped and ligated. In the photograph of the specimen (fig. 12), a complete apneumotosis of the right lower and subcardiac lobes is clearly visible. In the roentgenogram of the lung (fig. 13), the obstructing balloon is visible because of the sodium iodide solution

with which it is filled. The pulmonary arterial tree is uniformly injected with iodized oil. No differences can be made out between the atelectatic right lobe and subcardiac lobes and the other (normal) lobes. It is to be noted that the smallest arterioles are so clearly outlined that it seems highly improbable that the iodized oil could have penetrated the capillaries; for if the capillaries were filled we should expect a less clearcut and rather blurred roentgenogram.



Fig. 12 (dog C 52).—Postmortem specimen of the lung; the trachea was clamped before the chest was opened. The right lower and subcardiac lobes are completely atelectatic.

11. Atelectasis of the Left Lung: Dog C 51 was used in this experiment. The chest was opened, and intratracheal insufflation was employed. The experiment is particularly interesting because it shows the extraordinary resistance of the animal to a marked degree of obstruction of the pulmonary artery, and because the successive injections of iodized oil were followed by serial roentgenograms.

March 19, 1928: Iso-amyl-ethyl barbituric acid anesthesia was given. The left lower lobe was obstructed with our balloon.

March 20: A well developed atelectasis of the left lobe was noted; the heart shifted and the left lower lobe was hazy (fig. 14).

11:30 a. m.: Intraperitoneal anesthesia was given.

12:00 a. m.: The tube for intratracheal insufflation was introduced. An incision of the skin and of the soft parts was made from the manubrium to the mid-abdomen; hemostasis was made. The xyphoid process was dissected free, and the



Fig. 13 (dog C 52).—Roentgenogram of the lung showing the balloon obstructing the right lower and accessory lobes. The pulmonary arterial tree is uniformly injected with iodized oil. No differences can be made out between the atelectatic and the other (normal) lobes.

finger passed behind the sternum. Midsection of the sternum was performed. There was slight bone hemorrhage, and the left mammary vessels were ligated. A strong self-retaining retractor was used to separate the edges of the incision widely and so give a satisfactory view of the thoracic cavity. Intratracheal insufflation was established with an air pressure of 12 mm. of mercury. The heart beat was strong and regular. The left lower lobe was atelectatic, bluish black and did not expand with insufflation. The left upper lobe was of normal color and distended. The right lung was normal and distended. The subcardiac lobe

was visible under the heart and displaced toward the left side (represented by the clear triangle between the heart and the diaphragm in the roentgenogram).

1:00 p. m.: The animal was transported to the x-ray table. A cannula was introduced into the right jugular vein and 20 cc. of warm iodized oil was injected in one minute. A roentgenogram taken one minute (fig. 15) after the injection shows that the oil has penetrated the branch of the pulmonary artery to the atelectatic left lower lobe and that this branch is greater in diameter than that to the right lower lobe. (Compare this figure to figure 11, where the right lower branch is larger.)

Five minutes after injection, all branches of the pulmonary artery were seen to be injected and visible; the left lower branch was again seen to be dilated.

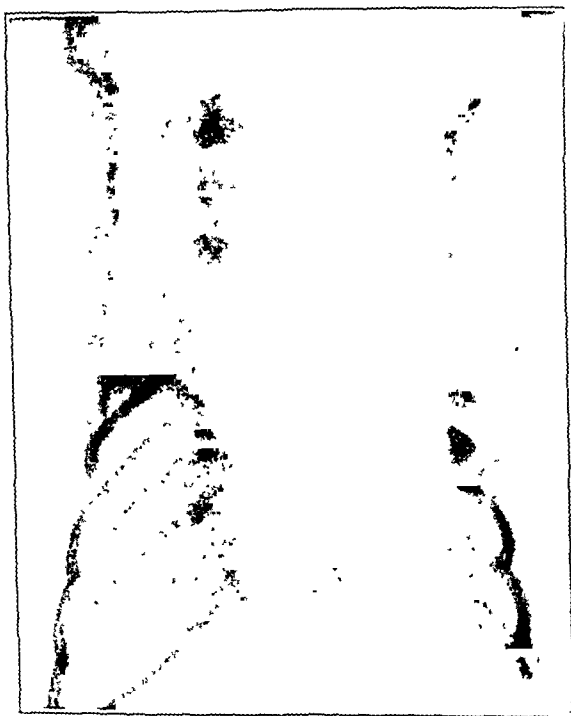


Fig. 14 (dog C 51).—Well developed atelectasis of the left lower lobe; the heart is drawn to the left and the left lower lobe is hazy.

1:07 p. m.: Ten cubic centimeters more of oil was injected. The dog was dyspneic, and the heart slowed down but was beating regularly.

1:40 p. m.: The heart action was weak and slow. After massage and intracardiac injection of epinephrine, it again became more rapid. Ten cubic centimeters more of oil was injected.

1:45 p. m.: The heart was beating even more slowly and finally stopped.

At postmortem examination, a clearcut apneumotosis of the left lower lobe only was seen (fig. 16). A roentgenogram of the lung (fig. 17) shows a perfect distribution of iodized oil in all branches of the pulmonary artery. No differences are apparent between the vessels in the affected and healthy lobes. The difference in diameters of the right and left pulmonary artery which shows up clearly in

the living animal is no longer apparent. In the same roentgenogram, the kidney of the animal shows that no iodized oil had penetrated this viscus.

III. Pneumonia of the Right Middle and Lower Lobes: Dog B 57 was used in this experiment.

March 30, 1928, 4:00 p. m.: Intraperitoneal anesthesia was given. Twenty cubic centimeters of a twenty-three hour culture in broth of pneumococcus type I was centrifugated, and the sediment suspended in 1 cc. of broth. This concentrated culture was insufflated into the right common bronchus through the bronchoscope



Fig. 15 (dog C 51).—Roentgenogram taken one minute after the injection of 20 cc. of iodized oil. Oil has penetrated the branch of the left pulmonary artery to the left lower lobe, and this branch (faintly shown in this particular figure) is greater in diameter than that to the right lower (normal) lobe. Compare with figure 11. The tracheal tube is seen in place.

March 31: The animal appeared very sick and toxic. The temperature was 103 F., pulse rate 90 and respirations 90. The right side was dull to percussion; there were diminished breathing and a few râles. The heart was markedly displaced to the right. In the roentgenogram (fig. 18) typical pneumonia of the right lower lobe is seen.

12:48 p. m.: Fifteen cubic centimeters of iodized oil was injected into the right jugular vein.

12:52 p. m.: Respiration slowed down after initial acceleration, and the heart stopped beating.

At postmortem examination, the chest was opened without previously clamping of the trachea. A greenish turbid fluid was found in both pleural cavities. A smear showed myriads of diplococci. The right, middle and lower lobes were of a dark reddish blue, airless and sank in water (fig. 8). A photograph of the specimen (posterior view) shows the involved lobes larger than the healthy ones because the trachea had not been clamped previous to opening the chest (fig. 19). A roentgenogram of the lung (fig. 20) shows no impairment in the circulation. It is impossible by this means to distinguish the healthy from the involved lobes.

IV. Pleurilobar Pneumonia: Dog B 56 was used in this experiment. Pneumonia was induced in the left lower and the right, middle and lower lobes. The process

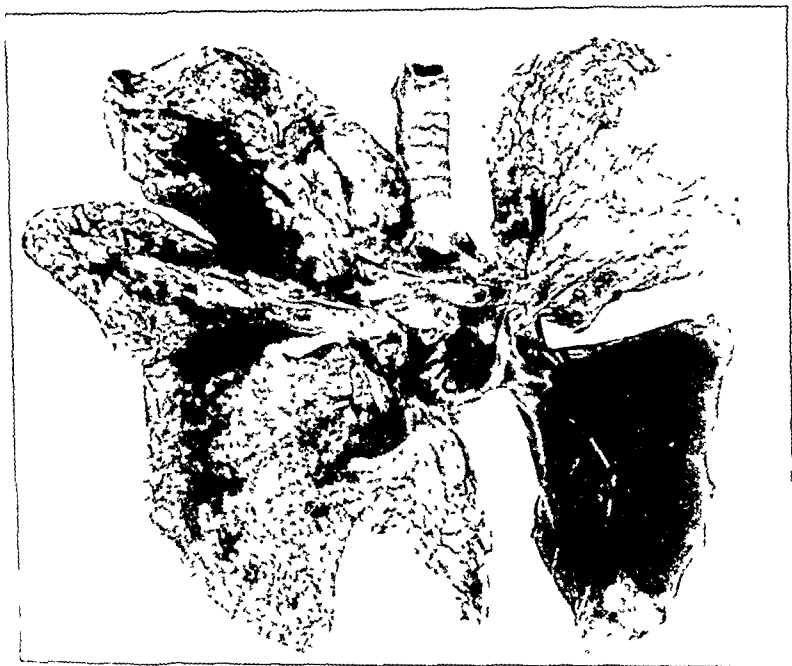


Fig. 16 (dog C 51).—Postmortem specimen showing complete atelectasis of the left lower lobe.

in the left lower lobe was probably seven days old or less and the process in the right lobe six days old or less.

March 27, 1928, 10:00 a. m.: Intraperitoneal anesthesia was given. Twelve cubic centimeters of twenty-hour old broth culture of pneumococcus type I was centrifuged, and the sediment taken up in 1 cc. of broth and insufflated into the left main bronchus through the bronchoscope.

March 28: The animal was not very sick.

March 29: The animal was rather sick. A roentgenogram showed haziness of the base of the left lung, shifting of the heart to the left without elevation of the diaphragm and a haziness of the base of the right lung.

April 5: The animal was very sick. The temperature was 100 F., pulse rate 166 and respirations 140. There was dulness over the right side of the chest



Fig. 17 (dog C 51).—Postmortem roentgenogram of the lung showing a perfect distribution of the oil in all branches of the pulmonary artery. No differences are apparent between the affected and the healthy lobes. The lower figure shows no iodized oil in the kidney of this animal.

and the base of the left lung. A roentgenogram (fig. 21) shows the heart now shifted to the right and the whole right side and the lower left side opaque. Intraperitoneal anesthesia was given. Twenty cubic centimeters of iodized oil was injected into the right jugular vein. The animal died within two minutes; that is, the respiration stopped after a minute, and the heart stopped beating after two minutes. In a roentgenogram (fig. 22) taken just before the heart stopped, the branch of the pulmonary artery going to the more involved lobe is again larger (right lower larger than the left). At postmortem examination, the aforementioned lobes were found to be consolidated and rather in the stage of gray hepatization (fig. 23). A roentgeno-

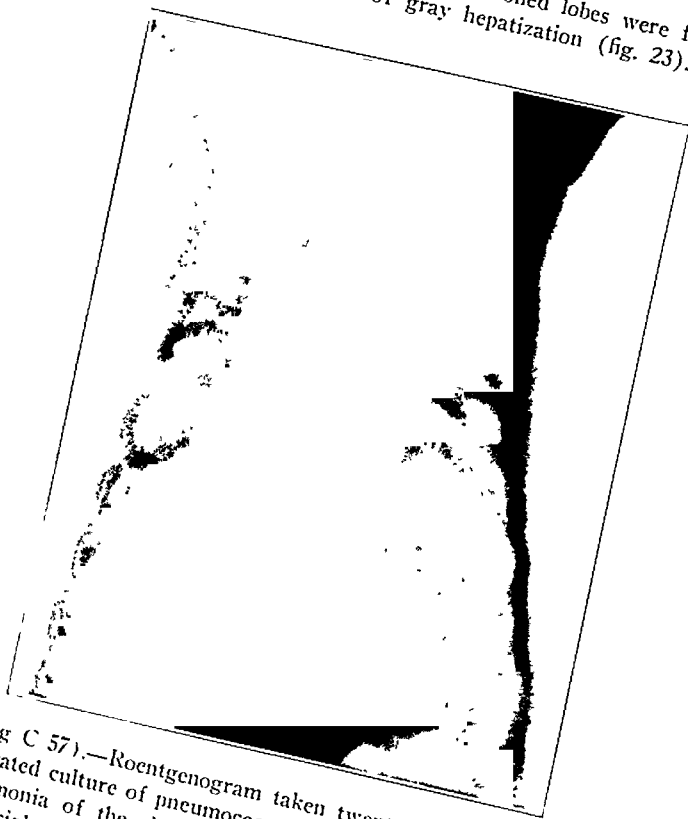


Fig. 18 (dog C 57).—Roentgenogram taken twenty-four hours after insufflation of concentrated culture of pneumococcus type I into the right main bronchus. A typical pneumonia of the right lower and middle lobe is seen; the heart is displaced to the right and the right side of the diaphragm is elevated.

gram of the lung (fig. 24) shows all the lobes well injected. No differences can be made out.

1. *Pneumonia of the Right Lower Lobe:* Dog 76 was used in this experiment. A roentgenogram was made of the heart. The same procedure was employed as for dog 56.
June 2, 1928, 1:15 p. m.: Thirty cubic centimeters of iodized oil was injected into the right jugular vein. Shallow and rapid breathing with cyanosis ensued.
1:18 p. m.: The shallow breathing stopped. The dog breathed deeply, and the heart beat was strong.

1:22 p. m.: There were deep agonal respirations, with the heart beating regularly at a rate of 100 per minute.

1:23 p. m.: The respiration stopped; the heart was still beating. After rhythmic traction on the tongue, respiration again started, deep at first for a



Fig. 19 (dog C 57).—Posterior view of lungs showing pneumonia of the right middle and lower lobes. The trachea is not clamped.

few respirations and then an alternating type with one deep and one shallow respiration.

1:27 p. m.: Respiration stopped.

1:28 p. m.: The heart stopped beating. The chest was opened, and the aorta clamped.

The roentgenograms of the lungs are not given here as they are similar to those already shown. The interesting feature in this experiment is that a roentgenogram of the heart (fig. 7) shows clearly that the right side is filled with iodized oil whereas the left side contains no trace of it. This experiment gave us the explanation of the peculiar phenomenon that the branches of the pulmonary artery were so well injected down to their finest ramifications; although relatively large amounts of oil were injected, the vessels appear clearcut and the lungs are not

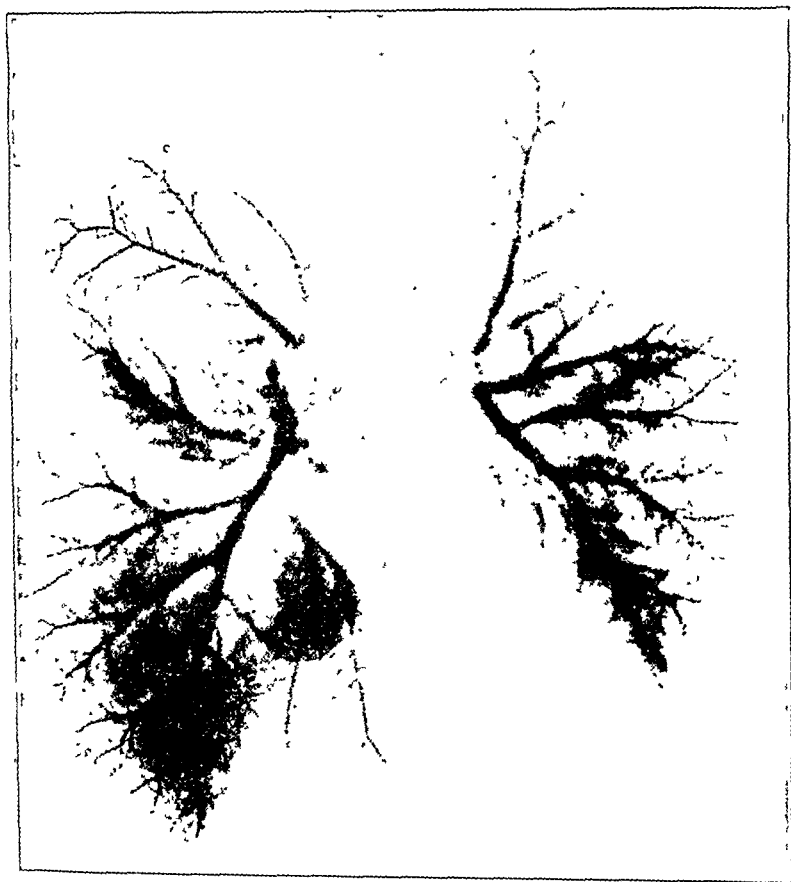


Fig. 20 (dog C 57) —Roentgenogram of the lungs extracted from the chest. The pneumonic right middle and lower lobes (indicated by arrows) are as well injected with iodized oil as the healthy lobes, it is impossible by this means to distinguish them.

diffusely opaque—an opacity which we should expect if the capillaries were injected with oil. We therefore suspected that iodized oil could pass through the precapillary arterioles, but could not penetrate the capillaries; the roentgenogram of the heart, of course, confirms this suspicion.

INJECTIONS OF INDIA INK

Only two cases will be shown here—one of atelectasis and one of lobar pneumonia, the other injections of this series being similar.

V. Atelectasis of the Right Lung: Dog B 83 was used in this experiment.

June 19, 1928: Intraperitoneal anesthesia was given. In order to produce a rapid atelectasis, the lung was insufflated with a stream of air saturated with ether (Connell insufflating apparatus) through the bronchoscope, and the right lower bronchus was obstructed with our balloon. Ten minutes later a partial atelectasis was apparent, and in one hour the atelectasis seemed complete.

Twenty-four hours later the right jugular vein was exposed and sectioned. A cannula was introduced into the distal end and one into the proximal end, as described under technic.

11:55 a. m.: The introduction of 1,000 cc. of Ringer's solution was started; the return flow of blood was light red. The heart action was rather weak, and 1 cc. of epinephrine was injected into the tube supplying Ringer's solution.

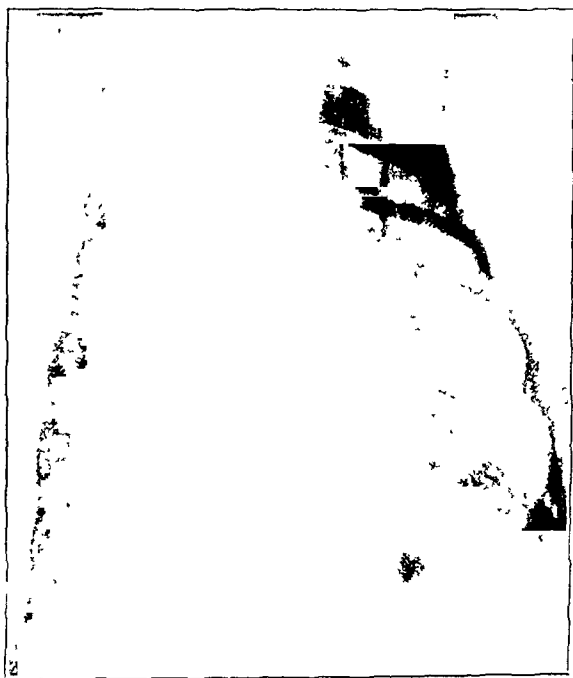


Fig. 21 (dog B 56).—Roentgenogram of the chest, showing pneumonia of the whole right lung, except the accessory lobe, and left lower lobe. Displacement of the heart to the right is less marked because of involvement of the left lower lobe as well.

12:00 a. m.: Ringer's solution was stopped and the injection of india ink solution started. Twelve seconds later, the return flow from the upper end of the jugular vein was completely black.

12:02 a. m.: The heart stopped beating.

The chest was opened. Both lungs were entirely black (fig. 25). The right middle and lower lobes and the subcardiac lobe were completely apneumatotic and sank readily in water (arrows in fig. 25). The right upper and left lobes were healthy and aerated. Specimens were cut from the different lobes and

tested in water. Four varieties were distinguished: *a*, floating; *b*, submerging; *c*, slowly sinking, and *d*, rapidly sinking. Sections were taken from each lobe. In cases of experimental atelectasis we find portions of the affected lobe with complete apneumatosiis and others in which the absorption of air is less complete. In other words, the results are similar to those in experimental or human pneumonia in which three stages of consolidation are distinguished: the so-called stage of engorgement, and red and gray hepatization; in the latter, areas of beginning resolution may also be seen.

Figure 26 is a photomicrograph of a section of healthy lung from this animal. Into the capillaries was injected india ink, so that the alveoli are clearly outlined

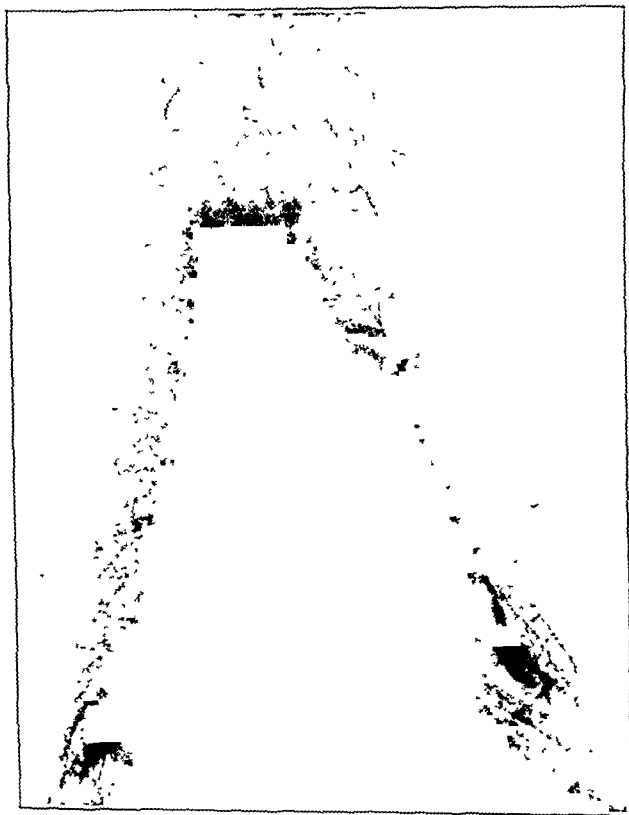


Fig. 22 (dog B 56).—Roentgenogram of the chest before the heart stopped shows the branch of the pulmonary artery to the more involved side (right middle and lower lobes) to be larger in diameter than the left.

by them. Notice the size of the alveoli for comparison with the following photomicrographs which have been made under the same magnification.

Figure 27 shows incomplete apneumatosiis. Alveoli with air are still visible, although the majority of them are shrunk and airless. The capillaries are tortuous, having followed the alveoli in the process of shrinkage. At first sight the circulation does not seem impaired, although the capillaries are somewhat decreased in diameter as shown by careful comparison with the capillaries in the previous photomicrograph. This is particularly well demonstrated when one

takes into consideration the fact that in a given area, say 1 square inch, the present photomicrograph shows twice as many capillaries, since 1 square inch of the present figure contains many more (shrunk) alveoli. Even if one considers that the lung in this state has more blood content per unit volume, nevertheless the blood content per alveolar sac is less and therefore the content for the whole lung is less than for a healthy lung.

Figure 28 shows a more advanced stage of atelectasis. Few alveoli still contain air; exudate is present. The capillaries are irregular and the blood content of the lung is certainly decreased.



Fig 23 (dog B 56).—Pneumonia in all the right lobes except the accessory; stage of early gray hepatization

Figure 29 shows the circulation still more impaired

An important fact is the simultaneous appearance, with the impairment of circulation, of dilated blood vessels the sizes of which increase in proportion to the circulatory impairment. We believe that these vessels do not represent dilated capillaries, as previously described by Bergamini and Shepherd, Santee, etc, but precapillary arterioles of the pulmonary artery which are dilated because of the resistance met with in the collapsed capillaries. This fact will explain the dilatation in the branches of the pulmonary artery corresponding to the affected lobe so clearly shown in the roentgenograms of the living animal with injections

of iodized oil (figs. 11, 15 and 22). It is of great interest to note in the following experiment that almost exactly the same phenomena were reproduced in cases of pneumonia.

III. Lobar Pneumonia: Dog B 82 was used in this experiment.

June 13, 1928: Intraperitoneal anesthesia was given. Fourteen cubic centimeters of a twenty-hour old broth culture of pneumococcus type I was centrifuged, the sediment taken up in 1 cc. of broth and insufflated into the left main bronchus with the bronchoscope.

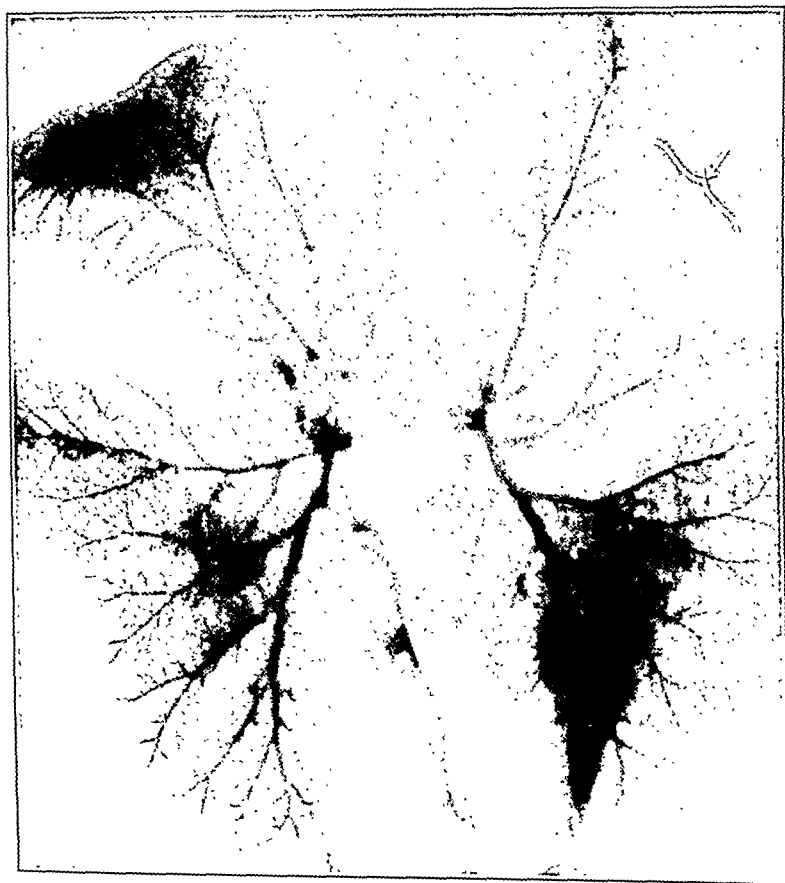


Fig. 24 (dog B 56)—Roentgenogram of lungs extracted from the chest after intrajugular injection of iodized oil. The involved lobes cannot be distinguished from normal lobes. Arrows indicate the healthy lobes.

June 14: The animal was very sick. Breathing was rapid and shallow. The roentgenogram (fig. 30) shows pneumonia in the left lung with complete shifting of the heart to the left and elevation of the left side of the diaphragm. The clear space between the heart and diaphragm is due to the encroachment of the subcardiac lobe on the left side of the chest.

11:50 a. m.: The jugular vein was exposed, sectioned and prepared as described under technic.

12:50 p. m.: Injection of Ringer's solution was started. Over a period of five minutes, 800 cc. was introduced; the return flow was about from 900 to 1,000 cc.

12:55 p. m.: The heart weakened. One cubic centimeter of epinephrine was introduced into the rubber tube going to the jugular vein cannula. The heart rapidly resumed its normal beat, but respiration became shallow and rapid. The outflow of blood from the peripheral cannula was still red but much lighter than at the beginning of the experiment. At this time about 1,000 cc. of Ringer's solution had been introduced. The Ringer's solution was now stopped, and the injection of india ink started and continued for one minute. Twelve seconds after

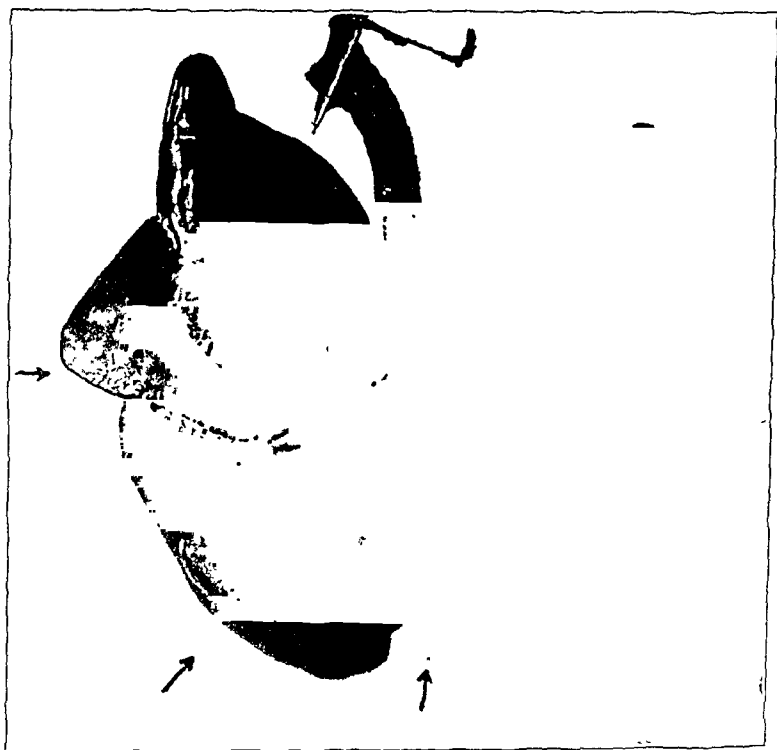


Fig. 25 (dog B 83).—Right atelectasis. Injection of india ink into the jugular vein. The arrows point to atelectatic lobes. All lobes are uniformly black.

the beginning of this injection, the return flow from the upper end of the jugular vein was completely black. Within one minute after the beginning of the injection, the heart stopped beating. The chest was opened and the large vessels of the base ligated. A photograph of the lung (fig. 31) shows it completely black; no differences in color are visible between the affected (left upper and lower) and healthy lobes (right). Specimens were taken and classified according to their behavior in a container with water as in the previous cases. Sections were made of these specimens and photomicrographs taken, the same magnification being used for all of them.

Figure 32 shows a section of a portion of the upper right lobe (normal). The large alveoli are outlined by the capillaries which are well injected with india ink. No dilated vessels are visible.

Figure 33 corresponds to the period of engorgement. This photomicrograph was made from a specimen which submerged but did not sink in water; the alveoli are shrunken but a great number of them are still air-containing. The diameter of the capillaries is decreased as compared with the previous figure. A few dilated vessels appear and these obviously cannot be capillaries because of

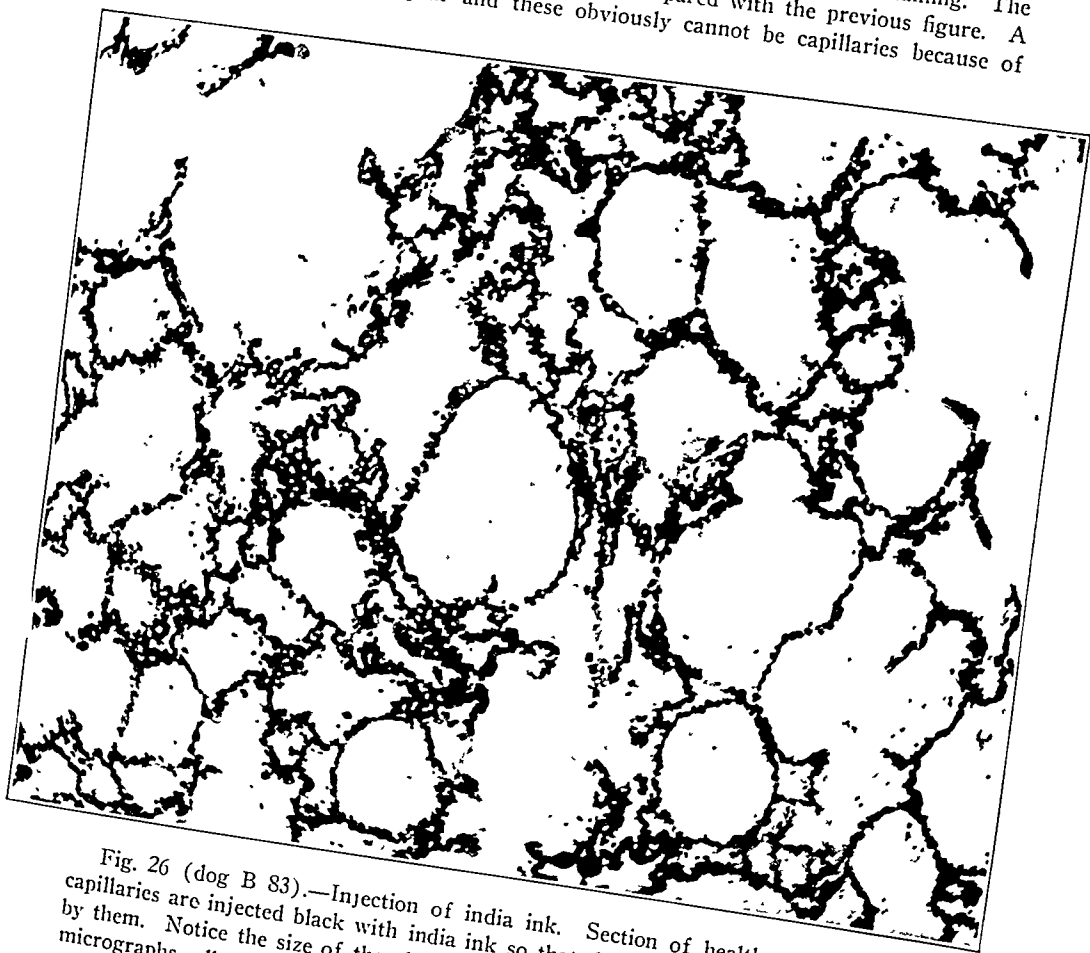


Fig. 26 (dog B 83).—Injection of india ink. Section of healthy lung. The capillaries are injected black with india ink so that the alveoli are clearly outlined by them. Notice the size of the alveoli for comparison with the following photomicrographs, all of which have been made under the same magnification.

their size; in our opinion they represent terminal branches of the pulmonary artery.

Figure 34 represents a more advanced period with exudate in alveoli. The capillary circulation is still more impaired. Cross-sections and longitudinal sections of dilated pulmonary arterioles are more clearly visible in this figure.

Figure 35 shows red hepatization (stained preparation) and complete airlessness of the alveoli. The capillaries are more irregular, and there are large areas

apparently without any capillaries. Sections of dilated arterioles are clearly visible.

Figure 36 shows gray hepatization. The circulation is more impaired, and the capillaries broken up. Sections of dilated arterioles are seen.

DISCUSSION

Before we comment on our observations, it will be necessary to see how the theory we propose agrees with the known facts on disturbances of gaseous exchanges in the lung in cases of inflammatory diseases of

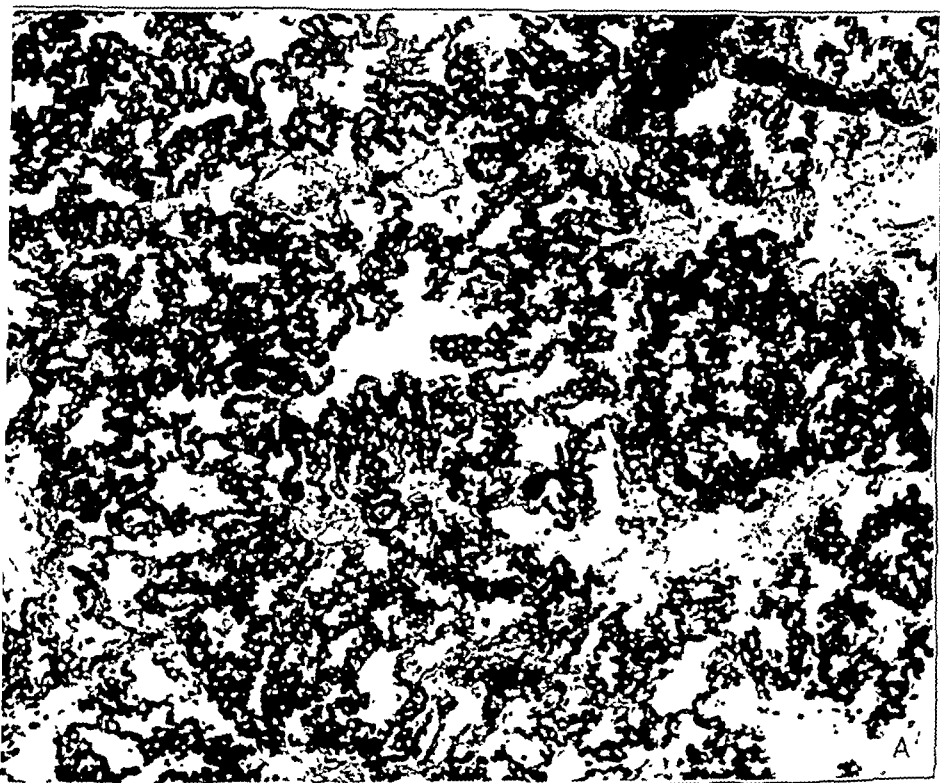


Fig. 27 (dog B 83).—Injection of india ink. Stage of incomplete atelectasis. Some alveoli with air are still visible, though the majority of them are shrunk and the capillaries tortuous.

the lung. We must inquire whether this conception of gradual and progressive circulatory impairment in the consolidated lung already severed from ventilation is in accordance with the modifications in the gas exchanges already noticed by other investigators in various cases of bronchial obstruction.

It is obvious that to the group of apneumatic lungs, in which after complete obstruction of a bronchus, absorption of the alveolar air and

collapse of the alveoli occur, we should add the cases in which partial obstruction of the respiratory ways produces a distention of alveoli, which are partially cut off from ventilation. In this last group belong asthma and emphysema.

If our conception is right,^{1,5} in these last cases circulation must remain intact or even be increased in the capillaries. Blood would circulate through channels insufficiently aerated and a marked reduction of oxygen with carbon dioxide retention in the blood should follow, because

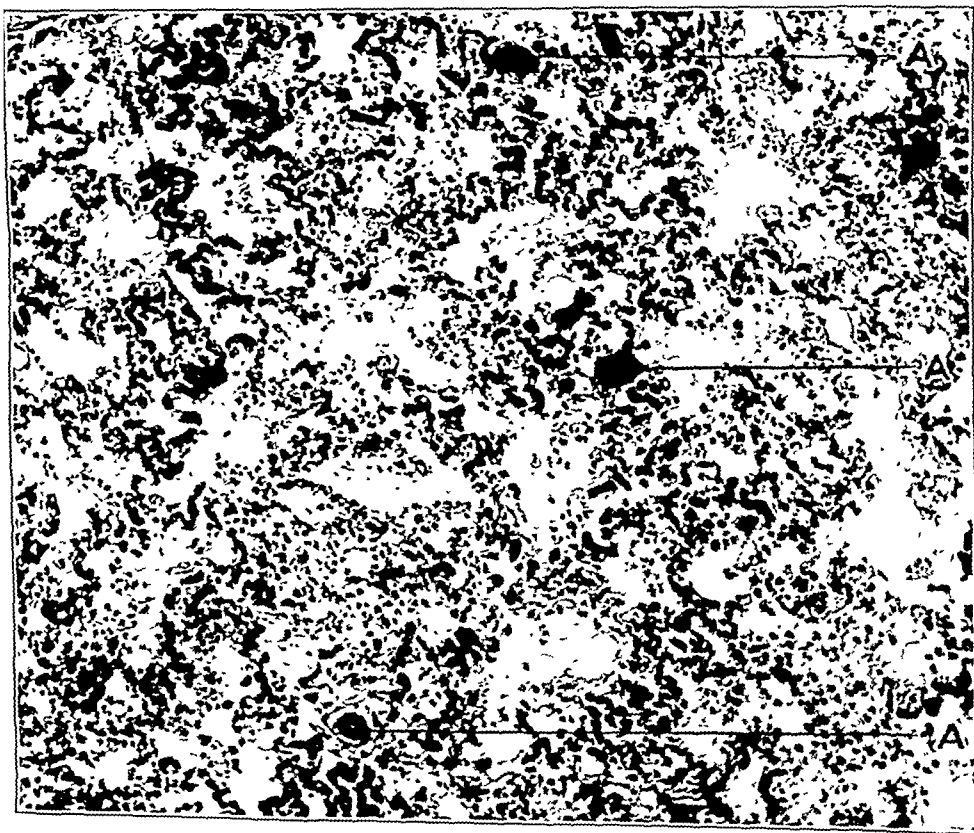


Fig. 28 (dog B 82).—More advanced stage of atelectasis. Few alveoli still contain air. Serous exudate is present. The capillaries are irregular and the blood content of the lung is certainly reduced; dilated arterioles are visible (A).

of the mixture of this unaerated with oxygenated blood. This is exactly what happens in asthma when bronchial spasm is extensive and involves the greater number of the bronchioli. Meakins has shown that in these cases the oxygen saturation of the arterial blood may be much below normal; an acute oxygen want with carbon dioxide retention develops, accompanied by pronounced hyperpnea and marked cyanosis.

In emphysema, where there is no bronchial obstruction but only impaired gas exchange because of structural changes in the respiratory channels of the lung (Hoover²¹), circulation is not affected. Oxygen want and carbon dioxide retention in marked cases are due to a relative stagnation of the alveolar air; this will have as a result a rise in carbon dioxide (from 60 to 63 mm. of mercury instead of 40 mm. of mercury) and a lowering of the oxygen partial pressure (from 70 to 75 mm. of

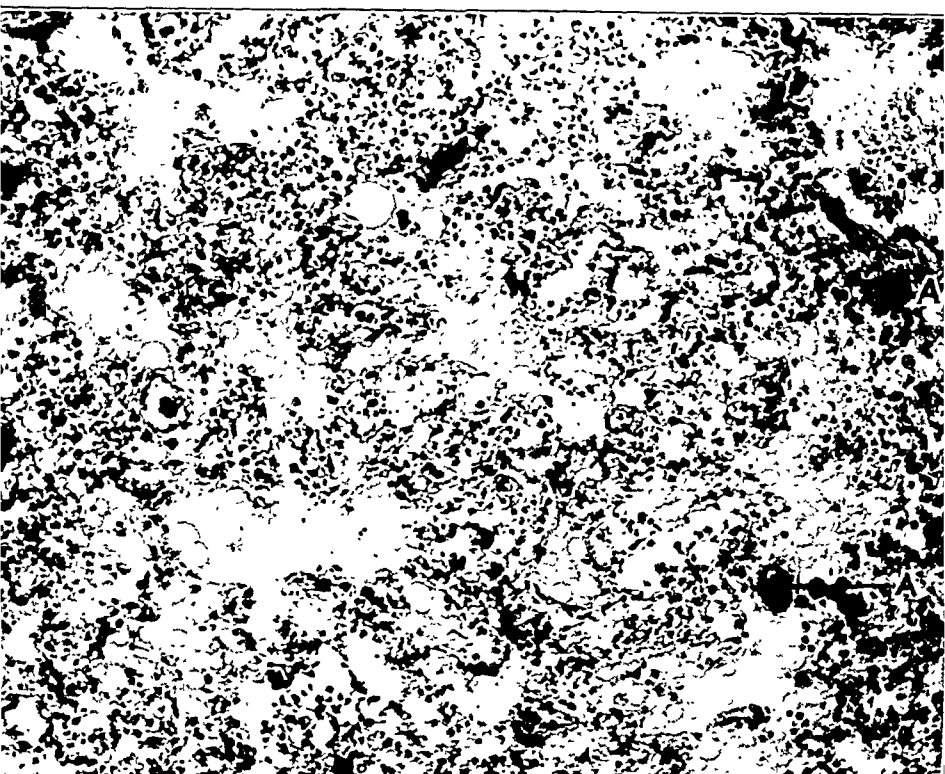


Fig. 29.—Atelectasis is more advanced than in figure 28. The circulation is markedly impaired. Dilated arterioles are visible (A).

mercury instead of 107 mm. of mercury) in the arterial blood. In both these diseases, as well as in acute edema of the lung, due, for example, to poisoning from phosgene gas (Winternitz and Lambert¹³⁹), the capillary circulation is intact, and the ventilation alone is impaired. More or less acute oxygen want with carbon dioxide retention, increase

139. Winternitz and Lambert: J. Exper. Med. 39:537, 1919.

in p_{H} and production of gaseous acidosis, is the characteristic modification in this group.

In opposition to the foregoing group are the conditions in which there is apneumatoxis of a considerable portion of the lung. Atelectasis, bronchopneumonia and lobar pneumonia belong in the last category. Acute bronchitis would stand between this and the former group, representing a transitional form between them.

In fact, in uncomplicated acute bronchitis, there is no change in the blood gases. "If however the process extends to the finer bronchi and

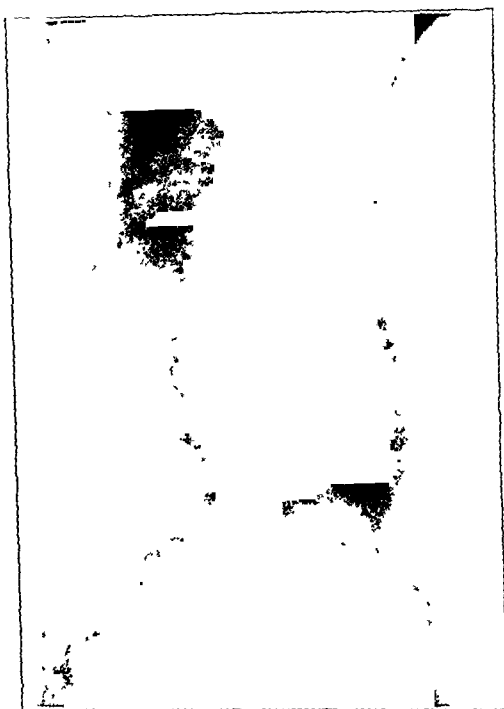


Fig. 30 (dog B 52).—Roentgenogram of the chest taken twenty-four hours after insufflation of pneumococcus culture. Pneumonia of the left lung with complete shifting of the heart to the left and elevation of the left side of the diaphragm is seen. The clear space between the heart and the left side of the diaphragm is due to encroachment of the subcardiac lobe on the left side of the chest.

involves the bronchioli and the alveoli, signs indicating interference with the proper aeration of the arterial blood and retention of carbon dioxide may develop" (Meakins and Davies¹⁰⁷). The degree of oxygen want will depend on whether "areas of lobules have been rendered non-functioning by closure of the bronchioli. As a consequence numerous small areas of the lung will be non-functionating, although a certain

amount of circulation will continue through these areas, in which oxygen tension will be reduced and venous blood will thus return to pollute the mixed arterial blood" (Meakins and Davies¹⁰⁷). Between uncomplicated bronchitis and bronchopneumonia the only difference would be, according to these authors, the existence or not of areas of lung cut off from aeration by obstruction of the corresponding bronchi or bronchioli. Furthermore, Hoover²¹ pointed out in 1918 the relation existing in these cases between blood flow and alveolar ventilation. Impairment of the circulation will follow bronchial obstruction and will gradually increase in parallel with the collapse of the alveoli. But in broncho-



Fig. 31 (dog B 82).—Injection of india ink into the jugular vein. Photograph of the lung specimen showing it uniformly injected black. Arrows point to pneumonic lobe (twenty-four hour old process).

pneumonia as against lobar pneumonia, there is a dispersion of the process all over the lungs, those patchy consolidations occurring irregularly in time and distribution. The result is that in a great portion of the parenchyma of the lung, especially in the severe cases as observed in influenza epidemics, circulation will be maintained through unaerated channels; this fact explains that there is a pronounced oxygen unsaturation with increase in carbon dioxide content of the blood. In these cases the administration of oxygen does not relieve, or only partially

relieves, cyanosis, and it may be inferred, according to Meakins and Davies,¹⁰⁷ that "a blockage of the lobules of the lung with impaired circulation is so pronounced as to prevent penetration of the oxygen into the alveoli, in spite of its increased partial pressure. If the cyanosis is somewhat relieved, this would indicate that certain of the alveoli are only partially obstructed." (See cases 1 and 3 in table XIII of Meakins and Davies,¹⁰⁷ page 208.)

We have mentioned the modifications in the gas exchanges in bronchitis and bronchopneumonia because they show the gradual transi-

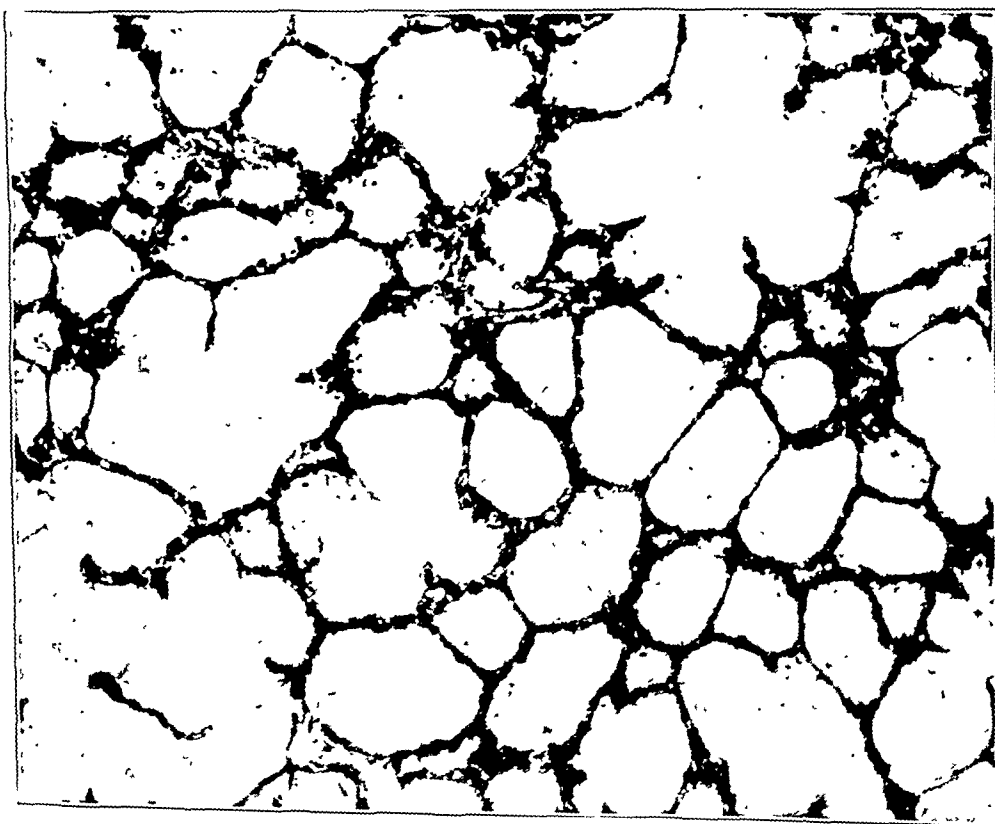


Fig. 32 (dog B 82).—Photomicrograph from the right upper lobe (normal). The alveoli are outlined by the capillaries which are well injected with india ink. No dilated vessels are visible.

tion from single bronchitis and bronchopneumonia and prove beyond doubt that occlusion of small bronchioli in the course of a bronchitis and the production of numerous patchy consolidations spread over the lungs determine interrelated changes in alveolar ventilation and capillary circulation, which give a simple explanation of the gas exchanges in these diseases.

In lobar pneumonia the same process occurs; but instead of a patchy and extensive distribution all over the lung, the process is strictly lobar. According to Meakins and Davies:¹⁰⁷

In the broncho-pneumonias the process is as a rule irregular in distribution and time. Thus various portions of the lungs become successively consolidated with obliteration of the alveoli. In lobar pneumonia a similar sequence of events occurs, but with this difference—that as a rule the pulmonary lesion progresses uniformly from partial to complete consolidation. It is therefore only when the

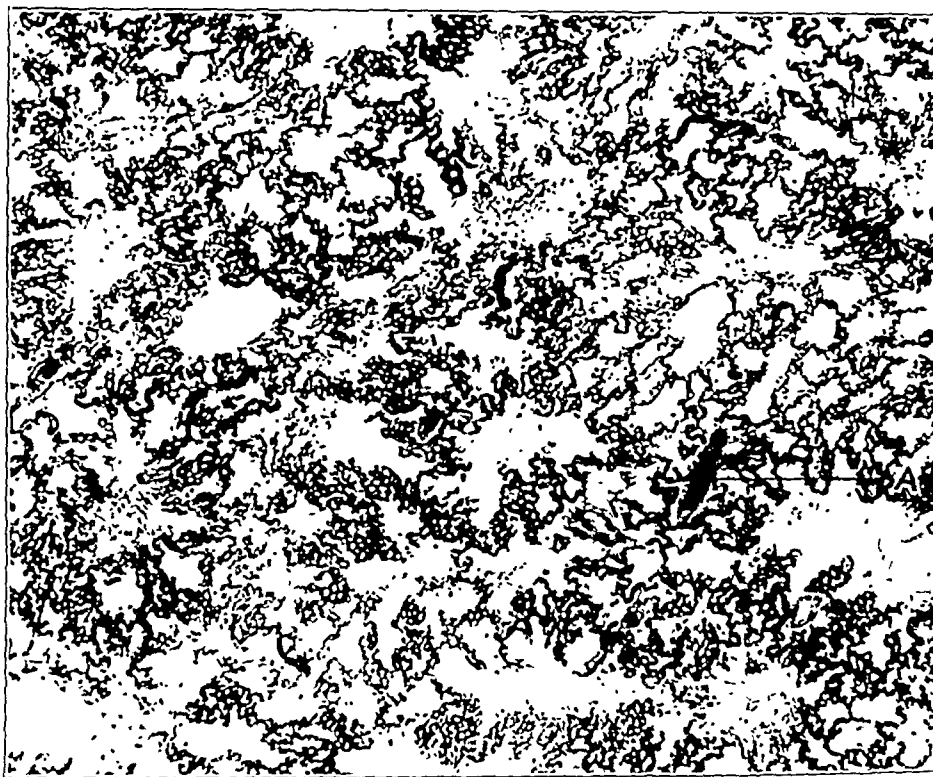


Fig. 33—This photomicrograph corresponds to the period of "engorgement" and was taken from a part of the pneumonic lung which submerged but did not sink in water. The alveoli are shrunken. The few dilated vessels seen are terminal branches of the pulmonary artery (*A*).

disease is observed from its earliest manifestations or when different lobes are involved in succession that the process of events may be determined.

We have maintained in previous papers¹³⁵ that the nature of the process is the same in bronchopneumonia or lobar pneumonia, the only difference being in the size of the occluded bronchi; and that from the standpoint of pathogenesis, bronchopneumonia bears the same relation to lobar pneumonia that patchy atelectasis bears to lobar atelectasis.

The altered gaseous exchange in pneumonia is an additional proof of this conception. In the early stages of pneumonia there is anoxemia combined with increase in carbon dioxide in the blood. In a case in which Meakins and Davies¹⁰⁷ had the rare opportunity to make observations before and after the disease (case 12, table xviii, page 226), they found in the arterial blood:

<i>O₂</i> per cent saturation of blood	<i>CO₂</i> per 100 cc. of blood
Before the onset.....	52
Second day of disease.....	67
Sixth day of disease.....	45
Seventh day of disease.....	47

Barach and Woodwell¹⁴⁰ reported a similar case, in which they noticed a sudden increase in carbon dioxide (from 53 to 61 per cent by volume) of the arterial blood coincident with the involvement of an additional lobe of the lung. Binger and Davis,¹⁴¹ in their case 15 (page 181), that of a young patient in the second day of pneumonia involving the middle and lower right and lower left lobes, failed to notice any changes in the oxygen saturation of the arterial blood although they had him in the oxygen chamber in an atmosphere of 40 per cent oxygen for more than an hour. They concluded that "in this instance we must assume that blood was circulating through unaerated portions of the lung, and that this rather than shallow breathing was in the main responsible for oxygen want." Case 16 of the same authors is similar to case 15. Unfortunately, the carbon dioxide content of the arterial blood is not given in these cases; both patients died on the second and fourth day after admission, respectively.

The high carbon dioxide content in the initial stages of lobar pneumonia is explained by Meakins and Davies¹⁰⁷ as being "due to early alveolar inflammation and interference with function occurring before the pulmonary circulation in these areas was grossly interfered with. There would therefore be a probable pollution of the arterial blood with venous blood rich in carbon dioxide." But although these authors accept that "the cases of broncho pneumonia are also of this type" (page 237), and that "the same conditions are operative in red hepatization of lobar pneumonia as exist in broncho pneumonia," they failed to see the identity of the pathogenesis in the two conditions, namely, bronchial obstruction. Our photomicrographs of the circulation in the early stages in lobar pneumonia show clearly this partial persistence of circulation.

140. Barach and Woodwell (footnote 122, first reference).
 141. Binger, C. A. L., and Davis, J. S.: The Relation of Anoxemia to the Type of Breathing in Pneumonia, *J. Clin. Investigation* 6:171 (Oct.) 1928.

On the contrary, as the process advances, the circulation in the consolidated lung will become more and more impaired. The amount of blood circulating in unaerated channels will be negligible, so that the percentage of carbon dioxide in the arterial blood will fall and that of oxygen rise toward normal. It is not within the scope of this work to discuss the relation between anoxemia, carbon dioxide content and shallow breathing. The only point which interests us is the increase

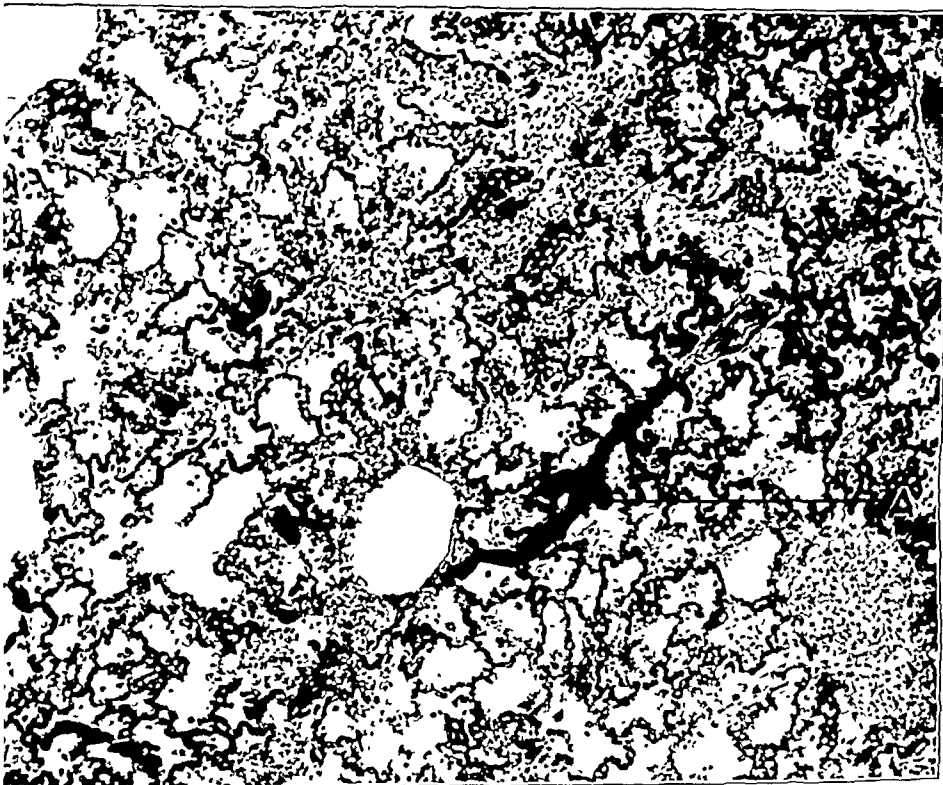


Fig. 34.—A more advanced process with exudate in the alveoli. Capillary circulation is still more impaired. Dilated pulmonary arterioles are clearly visible (*A*).

of carbon dioxide and fall in oxygen in the initial stages of lobar pneumonia and the decrease in carbon dioxide in the later stages of the disease.

These facts put beyond discussion the existence of a progressive circulatory impairment in lobar pneumonia, of the same type as in bronchopneumonia. This gradual circulatory impairment can be explained by the mechanism we proposed rather than the one proposed

by Binger¹⁴¹ or Kline and Winternitz.¹² It is interesting that Binger and Brow¹³⁶ remarked that "a close parallelism has been observed in radiographic shadow, physical signs and the volume of the functional residual air. The lung volume measured at normal expiration is diminished during the persistence of pathological signs in the lungs and returns to normal as the pathological signs disappear. The average time required, in cases which recovered, for the functional residual air to

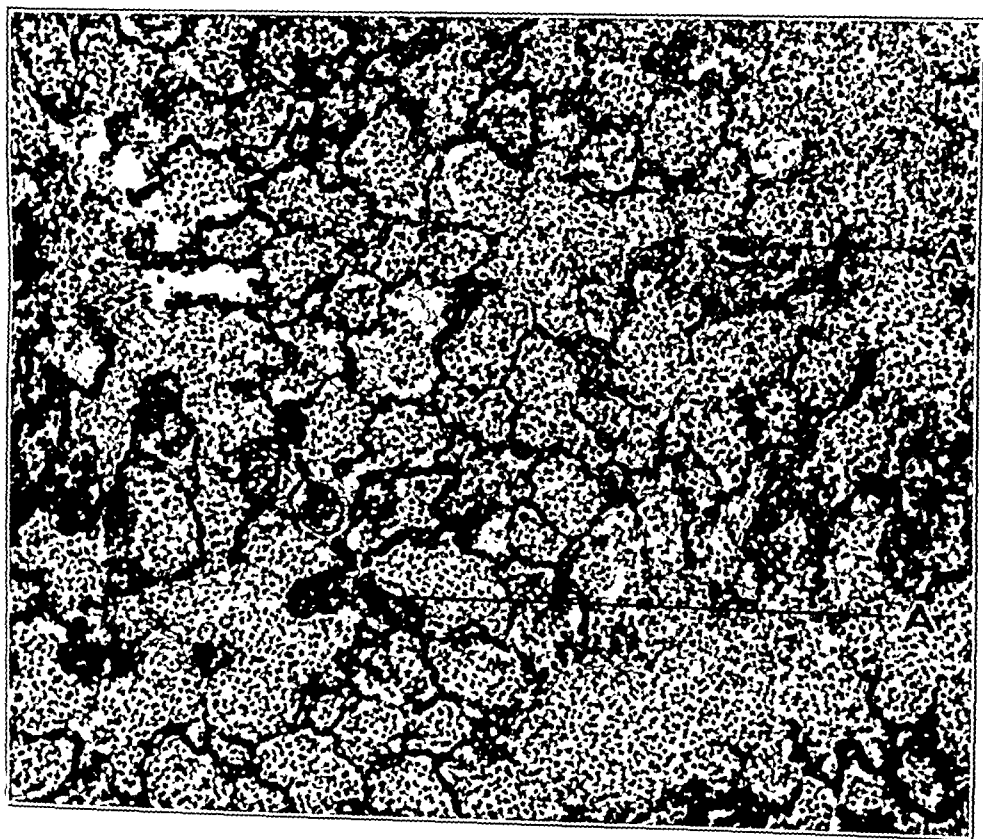


Fig. 35.—Stage of red hepatization (stained preparation). Capillaries are more irregular; there are large areas without capillaries. Dilated arterioles are clearly seen (A).

become constant was 11-12 days, counting from the onset of the disease." This being the case, it is difficult to understand how the cause of circulatory impairment would be the pressure exerted on the capillaries by the intra-alveolar exudate, and how the lung during the period of capillary compression would be smaller than under normal conditions. Likewise, the theory of thrombosis or embolism of the pulmonary vessels is untenable, for during red hepatization, when the fibrinous

process is at its height the circulatory impairment is conceded to be less pronounced than in gray hepatization.

Our conception, on the contrary, explains the progressive impairment of the circulation and is supported by facts demonstrable by simple experimental methods.

COMMENT

The observations given previously represent only a small part of our experimental investigation. We purposely refrain from mentioning

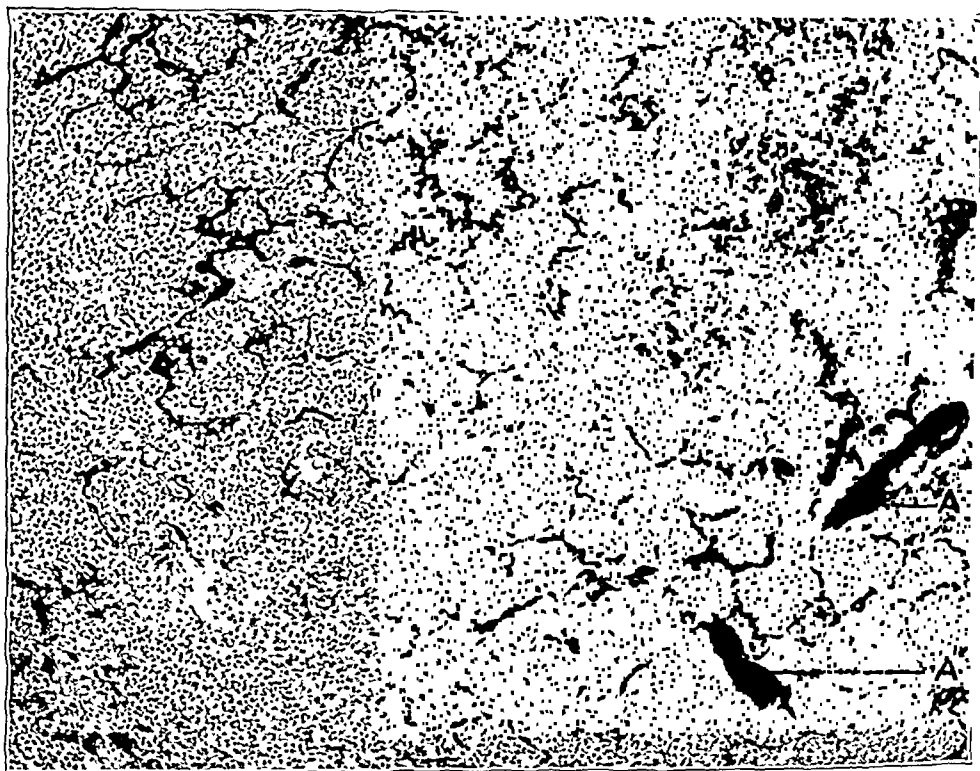


Fig. 36.—Stage of early gray hepatization. Capillary circulation is greatly impaired. The capillaries are broken up and sections of dilated arterioles are seen (stained preparation). Dilated arterioles are marked *A*.

results obtained with injections into the jugular vein of sodium iodide, vital stains, gelatin with radiopaque substances or even mercury. Experiments with these substances gave us a good insight into the causes of incomplete injections of the pulmonary tree of other authors which led to inaccurate conclusions. Gross,¹³ Binger¹⁴² and his collabo-

142. Binger and others (footnotes 132 and 136).

rators and Kline and Winternitz¹² have fallen into error on similar account. Postmortem injections into the lung, particularly in pneumonia, of gelatin or celloidin containing masses have failed to yield uniform injections. The incomplete injection may occur in a healthy lobe as well as in an involved one but more frequently in the latter because of postmortem thrombosis occurring more rapidly in the pneumonic than in the healthy lobe.

As our experiments have shown, it is important to distinguish branches of the pulmonary artery from the capillaries, when considering impairment of circulation in the lung rendered apneumatic from whatever cause. That is, the circulation in the arterioles is not impaired whereas in the capillaries it is. Moreover, when we talk about "an angiomatous condition" of an atelectatic lung we must remember that the capillary circulation is distinctly impaired in direct proportion to the degree of shrinkage and airlessness; however, because of this capillary impairment, there is a stasis in the small precapillary arterioles of the pulmonary arteries, and it is these arterioles which appear dilated in microscopic sections. In all our sections this fact was clearly visible. This fact is consistent with those roentgenograms of the chest taken during the injection of iodized oil into the jugular vein, which show the branch of the pulmonary artery corresponding to the involved lobe to be dilated.

We have given reasons for which we believe that the theories of thrombosis and embolism in the capillaries and arterioles of the pneumonic lung should be discarded. Thrombosis in the living human being or animal has never been proved nor has an acceptable explanation been given of the rapid restitution to normal of such large volumes of the pulmonary tissue in uncomplicated pneumonia.

The theory of compression of the capillaries by intra-alveolar exudate we believe to be no longer tenable. It is clearly shown in our photomicrographs that the alveoli filled with exudate are smaller than the normal ones.

The circulatory impairment in both the atelectatic and the pneumonic lung has been shown to be strikingly similar. This would point to a similar mechanism of production of such impairment, would explain the rapid reestablishment of the capillary circulation after aeration of the parenchyma of the lung in both diseases and would explain the absence of any marked lesions in the pulmonary tissue after recovery in uncomplicated cases.

These experimental, pathologic and clinical considerations lead us to make the following statement:

Circulatory changes are similar in the compressed atelectatic and consolidated (pneumonic) lung. They do not affect the pulmonary arterial tree but are exclusively limited to the capillaries. This capil-

lary impairment is not complete, blood in very reduced amounts circulating in the affected lung. It is proportionate to the degree of atelectasis and is due exclusively to the mechanical shrinkage accompanying the process of apneumatoses (atelectasis)—whatever the cause of this airlessness may be.

CONCLUSIONS

1. A new method for the study of the arterial and capillary circulations in the lung has been presented—intrajugular injections of iodized oil for the arterial circulation and Ringer's solution and india ink for the capillary circulation.

2. Circulation and ventilation of the lung are parallel functions; when ventilation is impaired circulation is decreased, and conversely.

3. In the compressed, atelectatic (apneumatic) and consolidated lung, the circulation is progressively impaired. This impairment is due to, and regulated by, the degree of collapse of the alveoli, and not to capillary thrombosis or capillary compression by alveolar exudate as heretofore believed.

4. Lobular pneumonia is comparable to lobular atelectasis and lobar pneumonia to lobar atelectasis; the circulatory changes are exactly the same, and they are related to impaired ventilation due to occlusion of a lobular or lobar bronchus with exudate; their clinical severity depends on the virulence of the microbes concerned.

5. In pneumonia and atelectasis, strikingly similar pictures are obtained so far as the evolution of circulatory impairment is concerned.

6. Only the capillary circulation is involved. Circulation in the pulmonary arterial tree is not affected. The capillary impairment is not complete.

7. Modifications in the gas exchange in pneumonia (oxygen and carbon dioxide) corroborate our experimental observations and theory.

8. Changes observed in the size of the alveoli in lobar pneumonia offer a new proof in favor of views, previously developed, that bronchopneumonia and lobar pneumonia should be considered as the infectious variety of patchy or lobar atelectasis, respectively.

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ABSTRACT OF DISCUSSION

DR. EMIL HOLMAN, San Francisco: As I understand Dr. Coryllos, he found no disturbance of the gross injection of the hemorrhagic consolidated lobe. In our injections, we found a definite cutting off of the vessels, a blocking of the entire precapillary circulatory bed. From his injections, there seems to be no difference at all.

We did not study microscopically the areas into which the injections were made. We felt that the filling up of the alveolar spaces and the closing up of

these alveolar spaces resulted in diminished circulation through the capillaries of the lung, and certainly through the precapillary circulatory bed.

DR. P. N. CORYLLOS, New York: I think that this discrepancy is due to the facts that we used iodized oil for our injections, and that we injected it into living animals and not dead ones, as in the experiments of Cross, Binger and his collaborators, and others. Iodized oil mixes with the blood and penetrates down into the smallest branches of the pulmonary artery, if the animal survives for a sufficient time after the injection. A minimum of from two to three minutes seems necessary for a successful injection. It is easy to understand that in injections into the pulmonary artery, on the dead animal with radiopaque substances, especially in suspension in gelatin, an obstruction of an important branch of the pulmonary artery can easily occur. This cause of error is eliminated, we believe, when the injections are made into the jugular vein of the living animal, without pressure and with a nontoxic substance; this passes through the jugular into the right side of the heart, which takes charge of its distribution into the lung. We are thus placed in conditions as near the normal as possible, and therefore we believe that the results obtained by this method may be considered as reliable.

THE SURGICAL TREATMENT OF BRONCHIAL ASTHMA *

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TABLE OF CONTENTS

The Problem of the Unrelieved Asthmatic Patient
Mechanism of the Asthmatic Paroxysm
The Bronchomotor Nerves of the Lungs
Operations for Bronchial Asthma
Analysis of Cases Recorded in the Literature
Report of Case
Suggestions for Further Investigation
Conclusions

THE PROBLEM OF THE UNRELIEVED ASTHMATIC PATIENT

The discovery of an allergic basis for certain cases of bronchial asthma and their striking cure based on this knowledge present one of the most fascinating chapters of modern medicine. However, this advance serves by contrast to emphasize the hopeless condition of those numerous unfortunate persons whose attacks continue unabated in spite of all medical treatment. As in other fields, the failure to relieve such sufferers has stimulated a far reaching search for alleviation. Thus, recently roentgen treatment has been added to the therapeutic possibilities for the internist. In certain instances roentgenotherapy has apparently been effective, but in many cases it, too, has failed. Pioneer surgeons also have attempted to solve the problem by using anatomico-physiologic knowledge developed by experimentation. Although certain surgical interventions for the relief of asthma, chiefly those directed toward the mobilization of the wall of the chest, date back for a considerable period of time, it is only within the last six years that an attempt has been made to influence a possible nervous control of the paroxysm. In this short interval, however, a number of operations have been tried which present important theoretical and practical phases. Several hundred cases of bronchial asthma in which operation was performed have now been mentioned in the literature, and a sufficient interval since the earliest of these now exists to allow a careful analysis of the results that have been obtained. Although in America

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fundamental contributions on the allergic basis of asthma have been made both in the experimental field and in the clinical applications of this knowledge, scant attention has been paid here to the possibilities of surgical assistance. And no adequate survey of the operative treatment for bronchial asthma is available in the American literature. It is our purpose in this paper to consider briefly the theoretical basis for such surgical interventions and to analyze the results so far obtained. We will discuss the mechanism of the asthmatic attack and the innervation of the lung only so far as they directly affect the rationale of the operative treatment. We recommend Alexander's¹ monograph on bronchial asthma for those interested in a detailed discussion of its pathogenesis, and Braeucker's² study of the extrinsic pulmonary nerves.

MECHANISM OF THE ASTHMATIC PAROXYSM

In attempting to relieve the paroxysms of dyspnea which characterize bronchial asthma by an operation on the extrinsic nerve supply of the lungs, it must be admitted at once that theory rather than fact is the basis from which the therapy originated. It is generally accepted that a diminished caliber of the finer air passages is the direct cause of the dyspnea. There are three factors that have been considered as possibilities in producing such a bronchial narrowing: (1) spasm of the intrinsic muscles, (2) mucosal swelling and (3) abnormal secretion. (The term "bronchial" here and elsewhere in this paper is used in its generic sense. It is intended primarily to signify the site at which partial stenosis may occur in the asthmatic paroxysm. The evidence is inconclusive whether this may be chiefly in the small bronchi or in the bronchioles.)

Bronchospasm.—The oldest theory, namely, bronchospasm, dates back at least to the early seventeenth century when Helmont³ suggested the "drawing together of the smallest bronchi" as the cause of the paroxysm, although the definite demonstration of the bronchial muscle came nearly two hundred years later in the classic work of Reissiesen⁴ (1822). After this discovery of a constricting mechanism in the respiratory tree, most investigators have taken it for granted that muscle spasm plays the predominant rôle in producing the asthmatic attack. This belief has been particularly strengthened by numerous experiments showing bronchial constriction on vagus stimulation. The original crude but ingenious methods of Wedemeyer⁵ in 1828 and Williams in 1840⁶ have been verified with greatly refined methods. However, when scrutinized from the point of view of proving that bronchospasm rather than mucosal swelling is the cause of the asthmatic paroxysm, little evidence has been offered. Most of the physiologic work in this field has determined only the increased resistance to air

movement through the respiratory tree after nerve stimulation and has not proved that nerve impulses acted on the bronchiolar muscle. In 1922 Huber and Koessler⁷ demonstrated hypertrophy of the bronchial muscles in asthma. This, in our opinion, is the most effective evidence in favor of the theory of bronchospasm. It is interesting that Strümpell,⁸ who favored mucosal swelling, stated in 1908 that the best proof of the bronchospastic theory would be such a demonstration. Most of the other facts that have been adduced in support of it, such as the therapeutic effect of atropine and epinephrine, can equally well be explained as due to a reaction on the vessels, the mucous membrane or the glands of the finer air passages.

Mucosal Edema.—Influenced by the character of the râles, Beau,⁹ in 1848, suggested mucosal swelling as the cause of the asthmatic paroxysm. This has been advocated by Blackley,¹⁰ Strümpell,⁸ Solis-Cohen¹¹ and others in correlating the fundamental pathologic process of asthma with that of urticaria and angioneurotic edema. This theory received rather scant attention until the recent important discovery of the allergic basis for at least certain types of asthma. Coca¹² particularly stressed the point that the outstanding pathologic lesion of atopy is edema. Consequently, he felt that swelling of the mucous membrane cannot be lightly dismissed. There is little direct evidence in its support. Postmortem examinations showing edema do not have the same weight as the demonstration of muscle hypertrophy because the former may be rapidly produced as a terminal complication, while the latter is evidence of a long continued process. Several bronchoscopic observers have found mucosal congestion and edema during an asthmatic paroxysm (Yankauer¹³ and Ephraim¹⁴). Because of the observation of mucosal swelling in the large bronchi, it is inferred that a similar condition exists in the smaller air passages. This inference is the only basis on which such observations can have any bearing on the cause of the paroxysm.

Secretion.—The characteristic sputum which frequently accompanies or follows a paroxysm of bronchial asthma has caused several authors to suggest an abnormal secretion as assisting mucosal swelling in the bronchostenosis. Curschmann,¹⁵ in 1883, suggested that the formed elements described by him played an important rôle in producing dyspnea. The exact significance of abnormal secretion in asthma is not known.

Summary.—Although the controversy over the mechanism of the asthmatic attack has been going on for a great many years, we seem no nearer a final decision in favor of any one hypothesis. In fact, there is strong presumptive evidence for each factor: bronchospasm, mucosal swelling and abnormal secretion (to a less extent). These factors are

probably present together in varying degrees. Consequently, we must freely admit that the underlying mechanism which produces the paroxysmal dyspnea is not definitely known. But all investigators agree that it acts by interfering with the freedom of air movement through the finer respiratory passages.

THE BRONCHOMOTOR NERVES OF THE LUNGS

All the factors that were discussed in the preceding paragraphs as possible causes of the asthmatic dyspnea are, at least in part, under the control of the extrinsic pulmonary nerves. It is this fact that has given rise to the hope that nerve interruption might benefit the disease. The various operations used have been grounded on the imperfect but increasing understanding of the complicated nervous connections and of the effects of stimuli traversing them. Consequently, it is important to review the present state of the knowledge concerning the anatomy and physiology of the nerve supply to the lung.

The vagus had long been considered the sole bronchomotor nerve of the lung. Stimulation of the distal cut end of the vagus causes bronchoconstriction on the same side (Longet¹⁶ and Dixon and Brodie¹⁷) and to a less extent on the opposite side (Weber¹⁸ and Braeucker²). This proves bilateral innervation. The specificity of parasympathetic stimulation in these observations may be questioned, as the experiments on which they are based were carried out in animals having a combined vagosympathetic trunk. It has been emphasized by Braeucker and Kummell¹⁹ that, in the dog at least, electrical stimulation limited to the vagus can only be obtained by application of the electrode to the nerve trunk within the skull. They found the result of such a stimulation to be usually constriction but occasionally dilatation or alternating constriction and dilatation. They admitted that this is not definite proof of two types of fibers in the vagus but that it might result from a difference in the tonus of the intrapulmonary autonomic plexus at different times. They regarded this plexus as the direct controlling motor center of bronchospasm.

The rôle of the sympathetic system in pulmonary innervation is even less clear. Unfortunately, from the point of view of simplicity, the schematic conception of the antagonism supposed to exist between the vagus and the sympathetic is inadequate to explain the known facts of lung innervation. Braeucker² stated that there are as many sympathetic fibers as vagal entering the posterior pulmonary plexus. Two theories are given in explanation of the beneficial effect of sympathetic interruption in the treatment of asthma: first, that bronchoconstrictor fibers run in the sympathetic chain as well as in the vagus, and second, that the sympathetic is the afferent side of a reflex arc. Kummell's²⁰ original operation on the extrinsic nerves for asthma was based on the

first theory. Dixon and Ransom²¹ obtained bronchoconstriction by sympathetic stimulation in cats, and Braeucker² has amplified this in the dog. Papilian and Cruceanu²² found in animals a decrease of the respiratory volume of one-half for from eight to ten days following cervical sympathectomy or painting the ganglions with 1 per cent nicotine. Weber¹⁸ showed that the bronchoconstrictor action of pilocarpine was prevented only after section of both vagi and the cervical cord. Frund²³ thought that the vagus and the sympathetic represent parts of the same vegetative nervous system, divided into tracts by more or less casual considerations, and one or the other may carry the principal mass of tonus-stimulating fibers. There is a wealth of opinion but a decided lack of fact in support of the second theory: namely, that the sympathetic is the afferent limb of a reflex arc of which the vagus forms the efferent or motor portion. Kaess,²⁴ Glaser,²⁵ Hesse,²⁶ Jungmann and Brüning²⁷ and Witzel²⁸ have assumed this theory. There is a close parallelism between the reflex arc hypothesis with interruption on the sensory side in bronchial asthma and the corresponding explanation offered for the operative results in angina pectoris. Gross anatomic study of the pulmonary nerves has long established the dual innervation to the lung. The finer histologic investigation has shown that the lung, like all other viscera supplied with autonomic motor nerves, has also an intrinsic (and probably automatic) system. The anatomic arrangement is most bewildering. The main bundles from the vagus are joined by numerous minute filaments from the sympathetic chain and from other intrathoracic plexuses and redistributed in a succession of bronchial and submucous plexuses. It is fortunate that apparently all those extrinsic nerve paths which control the caliber of the finer air passages are condensed in the posterior pulmonary plexuses.

Fontane and Hermann²⁹ preface their experimental study of denervation of the lung by a good review of the literature concerning the nervous structures in the lungs and their extrinsic connections. Remak,³⁰ in 1840, described separate ganglions among the fibers of the pulmonary plexuses. It was later shown by many observers that some of these ganglions are present in the bronchial walls and that there is a system of fine nerve fibers connecting them (Kandaraiki³¹ and Larsell³²). Frund²³ classified asthma into two groups, depending on the location of the stimulus producing bronchostenosis, (1) extrapulmonary and (2) intrapulmonary, and concluded that operation might do good in the first group. Braeucker² said that bronchospasm may theoretically occur after section of the posterior pulmonary plexus from stimulation of the ganglions in the bronchi either from the blood or through an intrapulmonary reflex arc. Brüning,²⁷ in 1927, expressed himself as favoring an intrapulmonary reflex. Herrmannsdorfer,³³

in discrediting operations on the vegetative system for bronchial asthma, stated that the many allergens which can induce asthma do so without invoking the extrinsic vagosympathetic mechanism. The success of nerve-interrupting operations in the treatment for bronchial asthma rests chiefly on the hypothesis that the activating agent of the broncho-stenosis does not produce its effect by a direct action on the bronchial mucosa or the peripheral nerve mechanism.

The many good and lasting results obtained seem to us strong evidence that in certain instances interruption of extrinsic nerve con-

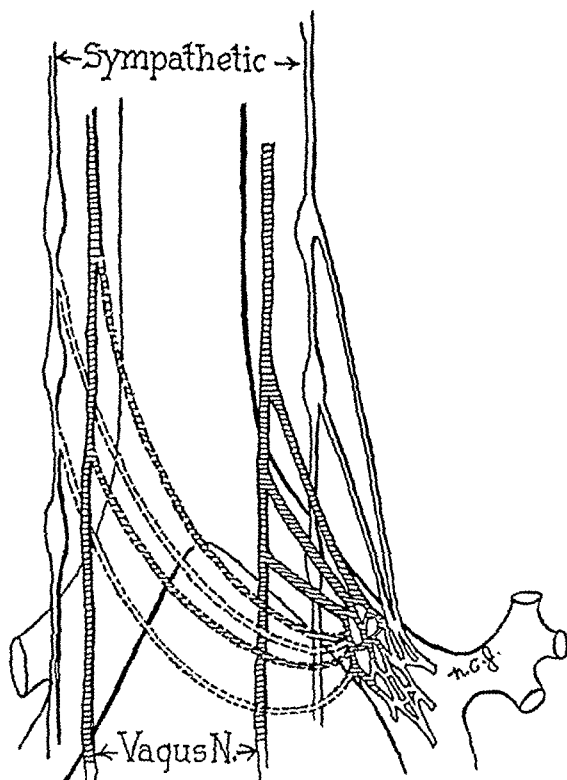


Fig. 1.—Schematic representation of the participation of both the sympathetic and the vagus fibers from the same side and from the opposite side in the formation of the posterior pulmonary plexus (according to Braeucker's experiments).

duction interferes with subsequent bronchostenosis. It is not known whether this acts by disconnecting the intrapulmonary muscles, vessels and glands from the central nervous system or by modifying in some manner the action of the intrinsic nerves.

Summary.—The rôle played by the extrinsic nerves of the lung in an asthmatic paroxysm is no clearer than is the local condition in the air passages that actually produces the stenosis. It is fair to state that there seems to be a bisystem, bilateral nerve supply to each lung, the

tracts of which are carried through the vagus and the sympathetic systems (fig. 1). The preponderance of opinion is in favor of the vagus as the main bronchomotor nerve. There is ample evidence that broncho-stenotic fibers are also carried over the sympathetic. That the sympathetic fibers are the inner or afferent side of a reflex arc is theoretically attractive without many known facts for its foundation.

OPERATIONS FOR BRONCHIAL ASTHMA

Operations on the Extrinsic Nerves of the Lung.—In 1923, Kümmell²⁰ surprised the surgical world by reporting immediate relief following the first intervention on the extrinsic nerve supply of the lung for bronchial asthma. He based his operation on the attempt to reduce bronchospasm by a decrease in motor innervation. He realized that the vagus was the chief motor nerve to the lung but feared the consequences of cutting it. Therefore, believing that some of the motor fibers of the vagus passed to the lung over the sympathetic, he performed a unilateral cervical sympathectomy. He apparently thought that in this way he would diminish the bronchospasm by weakening its innervation. Braeucker² in Kümmell's clinic then conducted anatomic and physiologic studies on the motor nerve paths to the lung. He found that stimulation of either the vagus or the sympathetic caused, at least at times, an increased resistance to the interchange of air. In other words this effect, commonly regarded as proof of bronchospasm, is represented in both systems. These data offer a more reasonable explanation for a possible diminution in the motor innervation following sympathectomy, and this explanation has been adopted by Kümmell.²⁰

Stimulated by the extremely optimistic report of Kümmell's first series many German, Russian and French surgeons began removing various parts of the cervicothoracic sympathetic system. As would be expected from such a wave of enthusiasm for an entirely new method of attacking asthma, the most varied results were recorded. Most of the brief reports of a few isolated cases that appeared in 1924 and 1925, though probably of some use at that time, are of practically no value in analyzing the operative results. They were prepared with too little data in regard to the conditions present. An even more unfortunate occurrence, the patients reported had been followed for too short an interval, in some instances only two weeks and usually not more than four months. Under such conditions it is obvious that many operations were carried out in entirely unsuitable cases, as, for example, instances of dyspnea due to cardiac insufficiency or to glandular involvement at the hilum. Also, the degree of completeness with which the sympathetic paths to the lung were interrupted was extremely variable. Even from the scant descriptions given of the operative technic, it was clear that many of these sympathectomies were incomplete. Even if complete removal of the stellate ganglion is achieved, sympathetic stimu-

lation reaches the homolateral lung, as the rami communicantes send fibers to it from as low as the fourth thoracic root (Braeucker²). One of the most striking facts about interventions on the sympathetic system for asthma has been the absolute divergence of their results in different clinics. Some investigators reported most encouraging results, while others saw no lasting benefit. Probably the selection of cases accounts for part of these differences. It seems to us impossible, however, to reconcile the complete lack of success of some with the brilliant and lasting results obtained by several in certain desperate cases except on the basis of incomplete application of the methods and technic advocated by the originators of these operations. On the other hand, it is equally obvious that sympathectomy is not a panacea for the relief of all dyspnea or even of all cases of idiopathic bronchial asthma.

Kümmell²⁰ removed the cervical sympathetic chain together with as much of the stellate ganglion as he could reach. Leriche and Fontaine,³⁵ on the other hand, felt that there was no necessity of removing more than the stellate ganglion. They operated through a cervical incision, though they suggested a thoracic attack on the sympathetic communications to the lung. So far as we have been able to ascertain, they have never carried out the latter procedure.

In a few instances bilateral cervical sympathectomy has been performed either at one sitting or with a short interval. The rationale of this procedure is that unilateral sympathectomy affects chiefly the nerve paths of the homolateral lung; consequently, the conditions on the other side are slightly changed. The year following Kümmell's first sympathectomy, Kappis³⁶ reported equally encouraging immediate results from vagotomy on the right side below the point of emergence of the recurrent laryngeal nerve. More than 100 patients have been operated on in this manner. Unfortunately, the results of vagotomy have never been reported as fully as those of sympathectomy. In 1924, Kappis stated that a sufficient number of patients had then been operated on both by sympathectomy and by vagotomy on which as a basis the results of these interventions could well be estimated in three or four years. Although this period of time has elapsed, as far as we can find such a report has not been published from his clinic. However, from the scant figures available, vagotomy results successfully in many instances. We now have the unusual phenomenon that interruption of either of two nerve pathways that were originally supposed to have predominantly antagonistic motor effects on the lung produce the same result in the relief of asthma. When this discrepancy became evident many investigators attempted to explain it on the basis of a reflex arc, of which the sympathetic is the afferent limb and the vagus the efferent.

Patients in whom either vagotomy or sympathectomy has failed have been treated by subsequent intervention on the other system, or in the

case of the sympathetic system on the other side. Though occasionally the treatment is a brilliant success, the majority of reports show this group to have the most disappointing results. This is probably due to the fact that included in it are all those cases in which relief cannot be obtained by operations on the extrinsic nerves. On the other hand, there is a small group in which both systems have been interrupted primarily. If the effect of intervention is the relief of bronchospasm and if the latter has a bisystem control, then such a removal of the nerve pathways of both systems is more logical than the interruption of either one alone. Or, if the beneficial effect of operation lies in the breaking of a reflex arc which has complicated multiple afferent and efferent paths, then the interruption of both sensory and motor channels is more likely to reduce the stimuli getting back to the lung than are operations on only one system. In short, if interruption on either the sympathetic or the vagus nerve is sometimes curative, sometimes ineffective, but frequently partially beneficial, then it seems reasonable that to combine these procedures may result in greater improvement than is obtained from either one alone.

Basing his observations on the experimental studies of Braeucker, Kümmell, in 1926, reported the isolation and section of the posterior pulmonary rami in asthmatic patients. According to the experimental work in animals, it was believed that by this operation all extrinsic control of bronchiolar constriction in one lung from both systems and from both sides was removed. As far as we can determine, in only three cases mentioned in the literature has this operation been performed with apparently good immediate results, though their final status requires a later report. As Kümmell said, on a carefully constructed preparation of the vagus and sympathetic fibers, one can see how they combine into one individual complex. This is the point at which the separation must take place to effect a maximum area of nonconductance (fig. 2). In this manner, also, the nerve supply to no other organ is involved. This is a point which is probably of no great importance for any one intervention but which may well be significant if the several nerve paths that contribute to this plexus had to be divided separately. Under this heading, then, we consider two different groups. In the first of these, the combined intervention is carried out because of the previous failure of a simpler one, and the outlook is not promising. In the other group, both systems are interrupted primarily because this is thought to be a logical procedure and the probabilities of relief seem more promising.

In addition to the foregoing operations which have been carried out and to that proposed by Leriche and Fontaine which has been mentioned, Daniélopolu³⁷ proposed a most complicated procedure of ramisection. It was designed to interrupt the sympathetic communications passing to the lung through the stellate ganglion while this

structure was conserved. One has only to read the description of this procedure to realize that it will probably never be carried out.

Operations on the Chest Wall.—W. A. Freund³⁸ was the first to suggest an operation to increase mobilization in the emphysematous type of chest, variously described as the rigid or fixed thorax. This was accomplished by a unilateral chondrectomy of a varying number of the costal cartilages, thus making it possible for increased excursion.

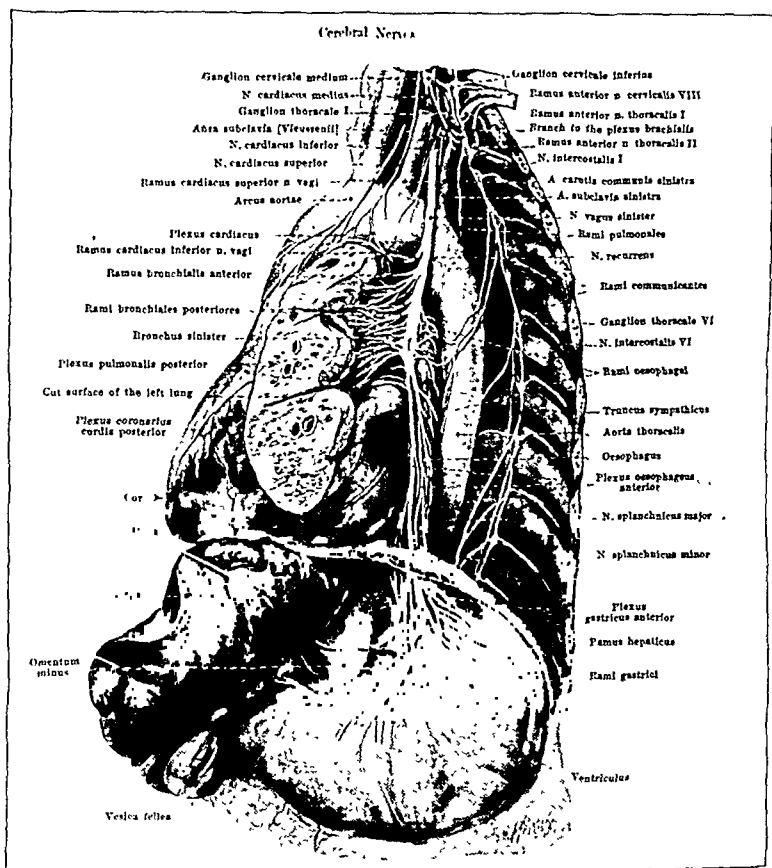


Fig. 2.—The extrinsic nerves to the left lung, showing the formation of the posterior pulmonary plexus, chiefly from branches arising from the main trunk of the vagus and joined by sympathetic fibers. From Spalteholz.

According to Bircher,³⁹ Freund's operation increases the vital capacity about 500 or 700 cc., on the average, while Heuer⁴⁰ referred to a maximal increase of 100 per cent. In one case, Bircher found chest expansion 10 cm. greater following unilateral excision of the second to the seventh cartilages. In 1918, he reported thirty cases of chondrectomy in which the patients had been under observation for several years, with the following results: cured (free from asthma and

bronchitis), 20 per cent; improved (lighter and less frequent attacks; able to work), 63 per cent; unimproved, 13 per cent; died, 3 per cent. Heuer assembled from the literature up to 1917 reports of about sixty cases in which Freund's operation had been carried out. Many of these showed recurrence of symptoms as fixation was reestablished. Although the patients were operated on by the old technic without destruction of the perichondrium, a few were still improved after three years. Failure, which occurred in the majority of these older patients and in some of Bircher's, was due to the reformation of the costal cartilages and consequent ankylosis at the point of resection. Several methods to prevent regeneration of cartilage were referred to by Bircher.¹⁹ Seidel advised the implantation of a muscle flap from the pectoralis major; Hoffmann covered the ends of the rib with perichondrium; Axhausen destroyed the latter with the cautery, and Bircher himself advised painting with carbolic acid. Several authors have mentioned the removal of the perichondrium, but this seems to us a more difficult method than inhibiting regeneration by the proper chemical cauterization. The work of Head⁴¹ on the prevention of rib regeneration by the use of Zenker's solution suggests its applicability in chondrectomy.

It seems paradoxical to suggest a posterior paravertebral thoracoplasty to increase the mobility of the hemithorax in the treatment of asthma and emphysema when the same operation is used to increase chest fixation in pulmonary tuberculosis. We will agree with Voelcker⁴² that a columnar posterior paravertebral thoracoplasty will change the direction of the ribs from the transverse position characteristic of emphysema to the downward slanting position of a normal chest or even to an exaggeration of the latter. However, this change of the angle of the ribs is accomplished at the expense of diminished chest capacity and ultimate increased fixation of the side operated on. Herrmannsdorfer²⁴ described a resection of the left second costal cartilage with anterior mediastinotomy for bronchial asthma. We do not see how this procedure would benefit the condition. This surgeon reported another operation in which an exeresis of the third to the seventh intercostal nerves on one side was combined with corresponding resection of the ribs. Such a procedure, like the posterior paravertebral thoracoplasty, decreases the size of the chest and increases its fixation. Intercostalectomy was used by Warstat⁴³ in 1917 to diminish movement of the lung in the treatment of chronic pulmonary tuberculosis. Therefore, these three operations suggested by Voelcker and Herrmannsdorfer seem to us irrational when applied to the treatment of asthma. Hirschberg⁴⁴ devised an operation to increase respiratory movements by a transverse division of the sternum between the second and third costal cartilages. He claimed an increase in vital capacity of from 400 to 500 cc. Braun⁴⁵ reported a case of emphysema in which this pro-

cedure produced relief and in which the condition had recurred following the older method of chondrectomy. This operation does not appeal to us as a substitute for chondrectomy with destruction of the perichondrium.

Miscellaneous Operations.—Several years ago, operations on the nose and throat had a great vogue in the treatment for bronchial asthma. The removal of part of one turbinate or the correction of some other slight abnormality in this region were among the first therapeutic attacks in a new case. There is little doubt that any irritative or infectious focus in the upper respiratory tract should be eradicated. Possibly in this way some patients in whom the condition appeared to be true bronchial asthma have been relieved. However, the accumulated experience both of the internist and of the rhinolaryngologist has shown that the vast majority of asthmatic patients receive no permanent benefit from such procedures. Thus, Sluder⁴⁰ stated that removal of polyps, resection of the nasal septum and treatment of the anterior nasal cells has never influenced asthma in his cases. Sterling⁴⁷ carefully reviewed the relationship of asthma to operations on the nose and throat and reported an analysis of 300 personal cases studied from this point of view. In 36 per cent of them, corrective operations were performed on the nose and throat for troubles which the patients as well as their family physicians considered to be the cause of the asthmatic syndrome. Only three of these 115 patients were free from asthma for two years following such operative intervention. In the rest, there was no effect on the asthmatic paroxysms. Rowe⁴⁸ limited the indications for operations on the nose and throat to the removal of infections detrimental to the general health. The latter is obviously indicated, and possibly certain lesions which might play the rôle of an irritative focus should be removed. However, a special examination of the nose and throat with corrections of such abnormalities as are really indicated is a part of the thorough investigation and medical treatment of the asthmatic patients which must be carried out in all instances before any operative procedures on the extrinsic nerves is considered.

Operations on the thyroid gland are in the same category. Obviously, if any part of the respiratory tree is encroached on in such a way as to diminish its lumen, this difficulty should be corrected if possible before the case is considered one of bronchial asthma. Paroxysmal dyspnea in the presence of a goiter should not be considered as idiopathic bronchial asthma until the continuance of respiratory difficulty has been demonstrated to persist after the correction of the tracheal compression. Likewise, certain instances of improvement in so-called bronchial asthma following roentgen therapy seem to us probably due to its effect on enlarged tracheobronchial glands. Splenec-

omy has been suggested for bronchial asthma by a Russian, Hynek,⁴⁹ in 1927. (This article was not available to us.) We have had no experience with this operation in asthma. Drey and Lössen⁵⁰ after accidentally discovering improvement of coexistent bronchial asthma following irradiation of the spleen for leukemia suggested a similar treatment for all asthmatic patients. A few optimistic results have been recorded by them and others. The history of therapy in asthma is replete with measures that have been used for a time, only to be found worthless later. This is well illustrated by Phillip⁵¹ who in 1818 reported twenty or thirty cures by the simple application of the galvanic current. The excessive enthusiasm which was first aroused by nerve

TABLE 1.—Operations

I. Operations on the Extrinsic Nerves of the Lung	
A. Sympathetic System	
1. Unilateral cervical sympathectomy (Kümmell) (including more or less of the stellate ganglion)	
2. Stellate ganglionectomy (Leriche)	
3. Bilateral cervical sympathectomy	
B. Vagus	
1. Unilateral vagotomy (Kapples)	
C. Combined Systems	
1. Unilateral or bilateral sympathectomy plus unilateral vagotomy	
2. Posterior pulmonary plexus resection (Kümmell)	
D. Proposed Operations (not carried out as far as known)	
1. Ramisection of the first four thoracic rami communicantes (Leriche)	
2. Cervical sympathectomy, severing all fibers of vagus and superior laryngeal nerves entering the thorax, cutting rami communicantes connecting the inferior cervical ganglion with the first thoracic nerve and with the sixth, seventh and eighth cervical nerves (Danklopolu)	
II. Operations on the Wall of the Chest	
1. Chondrectomy (Freund)	
2. Posterior paravertebral thoracoplasty (Voelcker)	
3. Anterior mediastinotomy (Herrmanns-förfer)	
4. Excision of intercostal nerves 3 to 7, plus rib resection 3 to 7 (Herrmanns-förfer)	
5. Transverse division of the sternum between the second and third cartilages (Hirschberg)	
III. Miscellaneous Operations	
1. Nose and throat, thyroid, etc.	
2. Splenectomy	

resection, for example, is no indication that it will ultimately have a definite place in the treatment of asthma. However, there seems to be little theoretically to recommend the possibility of preventing the asthmatic paroxysm by removal of the spleen. We feel that resection of the extrinsic nerves offers much more as an experimental operation than splenectomy or the removal of any other visceral organ.

Table 1 shows the more important operations suggested for the treatment of bronchial asthma. It is seen in going over this table that in grouping the cases a condensation into a simplified system is desirable. In fact, if each variation of operation on the sympathetic nervous system carried out by the individual operators was classified separately, the list of operations would be nearly as long as the list of operators. Consequently, we propose the simplified classification given in table 2

as a basis for studying the results of operative procedures in bronchial asthma.

ANALYSIS OF CASES RECORDED IN THE LITERATURE

Although the points described in the previous sections are of theoretical interest and frequently suggest rational therapy, the final test of any measure undertaken is the relief obtained from the asthmatic paroxysms. Does intervention on the extrinsic nerves offer any hope for those sufferers who have not been relieved by all of the usual medical methods, including particularly those of allergy? The results already obtained should be our guide in further efforts along this line. As recorded in the literature, in several hundred cases of bronchial asthma operations have already been performed on either the sympathetic or the parasympathetic system. Unfortunately, most of these have been inadequately reported. With the wave of enthusiasm that followed the pioneer work of Kümmell and Kappis in this field, many surgeons hastened to record a few cases without allowing an interval

TABLE 2.—*Basis for Studying Results of Operative Procedures in Bronchial Asthma*

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- | | |
|----|--|
| 1. | Interruption of the sympathetic |
| 2. | Interruption of the vagus |
| 3. | Interruption of both sympathetic and vagus |
| | A. Primary |
| | B. Secondary (previous operative failures) |
| 4. | Restoration of respiratory excursion |
-

sufficient to judge of the results. We feel that six months is the shortest period that makes the case worthy of any consideration in a statistical study. The majority of these cases followed this long are reported only in groups without details. This is a particularly unfortunate circumstance in bronchial asthma, because during this period many instances of dyspnea due to cardiac disease, to enlargement of the tracheal glands, or to other extraneous causes were undoubtedly included in the group in which operation was performed. A careful search of the literature, in fact, reveals only 29 detailed cases out of more than 300 patients operated on in which the results six months after operation are stated. We have assembled these in table 3.

It has seemed to us desirable to study the results collected from the literature in two different ways: (1) the assembly in a table of all cases reported in detail in which the result at least six months after operation is given; (2) the presentation of the statistics from the few clinics that have reported a considerable experience with these operations. As a matter of fact, it will be found that these two methods of analytical study lead to similar general conclusions. Each of them has certain points of advantage. The table of assorted cases has the obvious disadvantage that it is not a representative cross-section of the experi-

ence with these operations. In general, the successful case is much more apt to be reported than the unsuccessful one. On the other hand, it can be fairly contended that an operation so intricate in its technic as the total removal of the stellate ganglion, attempted by a large group of surgeons without particular experience along this line, will result in a high percentage of incomplete removals. Though both of these points are valid, still the case reports are of definite value and have the merit of being collected from a variety of sources. The chief objection to the second method is that the enthusiasm or prejudice of the particular clinic may color the expression of the results obtained. However, this method has the especial merit that it presents all of the results of a fairly extensive series and that it shows the disadvantages and complications as well as the advantages. The conclusions obtained from these two methods of study will be correlated. Only twenty-nine cases have been found acceptable for detailed analysis of results in bronchial asthma following operations on the vagus and the sympathetic nerves.

Table 4 is a résumé of the results in the individual cases included in table 3.

We may summarize, then, by stating that there are a few brilliant cures in extremely severe forms of asthma. Roughly, one half of the patients have been definitely improved, while frequently the other half, after temporary improvement, are in no better condition than before operation. The patients who were cured have been followed on the average almost two years. In some of these the condition may, of course, recur at a later date. However, when it is realized that in these patients the condition was, almost without exception, hopeless from the medical standpoint and that nothing was done to relieve the severe emphysema usually present, this is not altogether a discouraging outlook for the further trial of the operative method. Undoubtedly, a number of cases are excluded from the table on account of lack of the sufficiently long postoperative interval, in which the asthmatic attacks had already recurred. These are balanced, however, by a number of promising cases that had not been followed long enough to be included. Also, the occurrence of attacks for a short period after operation is compatible with ultimate relief as is shown in some of the cases cited. Furthermore, in a great many instances sympathectomy had been carried out on only one side. A number of examples are found in the table in which unilateral sympathectomy was followed by recurrence, while a similar procedure on the second side produced complete disappearance of the asthmatic paroxysms.

Turning from the disappointingly small number of cases reported in sufficient detail to permit individual study, we now review the results reported from individual clinics in which twenty or more operations

TABLE 3.—Results of Extrinsic Nerve Operations in Individual Cases (From the Literature)

Reporter	Year	Age	Sex	Clinical Data	Operation	Date	Result	Observation Interval	The Authors' Impression
1. Hesse..... (footnote 26)	1925	23	M	Asthma 15 years; roentgen therapy without relief; emphysema	Right cervical sympathectomy (total)	2/ 3/24	No attacks	19 mo.	Good result
2. Hesse.....	1925	24	M	Asthma 22 years; emphysema	Right total cervical sym- patectomy	1/12/24	Complete relief Unimproved	8 mo. 19 mo.	Shows necessity of long follow-up
3. Hesse.....	1925	54	M	Asthma 13 years; rigid thorax; emphysema	Right cervical sympathectomy	4/ 2/24	Asthmatic attacks; no attacks (5 mo.)	9 mo. 14 mo.	Difficult to classify
4. Hesse.....	1925	40	F	Asthma 20 years; emphysema	Left cervical sympathectomy	6/21/24	No real attacks	15 mo.	Good result
5. Hesse.....	1926	30	F	Severe asthma 2 years; emphysema	Right sym- patectomy	9/17/23	Recurrence	2 mo.	Failure after single and good result following double sympathectomy
6. Hesse	1926	24	M	Asthma 16 years; emphysema	Left sym- patectomy	3/ 8/24	No attacks	25 mo.
7. Hesse.....	1926	23	M	Asthma 3 years; emphysema; chronic bronchitis	Right sym- patectomy	10/30/24	Recurrence	11 mo.	Failure of unilateral sympathectomy; not improved by bilateral
8. Hesse.....	1926	59	F	Asthma 13 years; emphysema; chronic bronchitis	Left sym- patectomy	11/28/24	Unimproved	1 mo.	Failure of bilateral operation
9. Hesse.....	1926	40	M	Asthma 15 years; emphysema; chronic bronchitis	Right sym- patectomy	10/30/24	Unimproved	11 mo.	
10. Hesse.....	1926	17	M	Severe asthma 15 years; emphysema; chronic bronchitis	Left sym- patectomy	12/10/24	Recurrence	2 mo.	Failure of bilateral operation
11. Hesse.....	1926	16	M	Asthma 12 years; chronic pneumonia	Right sym- patectomy	6/23/25	Unimproved	10 mo. after first operation	
12. Hesse.....	1926	40	F	Severe asthma 7 years; continuous attacks 2 months	Left sym- patectomy	12/10/24	Unimproved	Failure of bilateral sympathectomy
13. Hesse.....	1926	47	F	Asthma 9 years; chronic bronchitis; emphysema	Right sym- patectomy	1/17/25	Unimproved	11 mo.	
						12/23/24	No attacks	5 mo.	Question of chronic lung suppuration
						3/ 5/25	Unimproved	12 mo.	Value of long obser- vation
						4/19 25	No attacks Recurred	8 mo. 1 yr.	
							Improved	7 mo.	

14. Hesse.....	1926	51	M	Asthma 23 years; chronic bronchitis; emphysema	Right sympathectomy	3/21/25	No attacks; nocturnal dyspnea	12 mo.	Suggests chondrectomy
15. Hesse.....	1926	40	M	Asthma 15 years; chronic fibrosis; pneumonia; chronic bronchitis	Right sympathectomy	4/11/25	Unimproved	12 mo.	Question of chronic lung suppuration
16. Hesse.....	1926	29	F	Severe asthma 2 years; chronic bronchitis; emphysema	Left sympathectomy	10/ 7/25	No attacks	6 mo.	
17. Leriche and Fontaine (footnote 35)	1926	45	F	Severe asthma 2 years; bedridden	Left stellate ganglionectomy	3/11/25	No attacks	36 mo.	Striking result
18. Leriche and Fontaine	1925	45	F	Asthma 6 years; exophthalmic goiter	Left stellate ganglionectomy	9/ 9/25	No attacks	30 mo.	Good result
19. Leriche and Fontaine	1927	51	M	Asthma 1 year; bronchitis; rigid thorax	Left stellate ganglionectomy	1/ 9/26	Unimproved	27 mo.	Suggests chondrectomy rather than nerve operation
20. Leriche and Fontaine	1927	55	M	Severe asthma; rigid thorax	Chondrectomy	1/ 5/27	Increased expansion; attacks persist	Relief by combination of chondrectomy, stellate ganglionectomy and vagotomy
21. Kümmell, H., Jr. (Beitr. z. klin. Chir. 132 : 249, 1924)	1924	57	F	Asthma 12 years; emphysema	Left stellate ganglionectomy Right vagotomy Left sympathectomy	3/ 2/27 3-28/27	Free from attacks Recurrence within 5 months	10 mo.	Follow-up too short
22. Rameriz and Pool.... (J. A. M. A. 84 : 2002 [June 27] 1925)	1925	39	F	Asthma 2 years; chronic bronchitis; emphysema; pulmonary fibrosis (x-ray)	Right sympathectomy Right superior sympathectomy	?	No attacks	9 mo. after first operation	Incomplete operation; roentgenogram suggests intrapulmonary pathologic change
23. Rameriz and Pool....	1925	55	M	Asthma; chronic bronchitis; emphysema	Right cervical sympathectomy	9/18, 24	Unimproved	7 mo.	
24. Hartung (Centralbl. f. Chir. 51 : 2360, 1924)	1924	37	M	Asthma 11 years	Left sympathectomy	6/12/24	Unimproved	10 mo.	
25. Kroll (Deutsche med. Wochenschr. 51 : 1323, 1927; Centralbl. f. Chir. 54 : 1885, 1927)	1927	?	?	Asthma 2 years	Left sympathectomy	10/21/	Good result	6 mo.	
26. Lutz (Centralbl. f. Chir. 54 : 1885, 1927)	1927	31	?	Asthma since infancy	Left sympathectomy	2/24/	Improved	30 mo.	Complication paresis left upper extremity
27. Lutz.....	1927	57	?	Severe asthma for several decades	Total sympathectomy	1/27/	No attacks	7 mo.	
28. Döttner (Med. Klin. 21 : 197, 1925)	1925	37	M	Asthma 20 years; roentgen therapy without help	Left sympathectomy	?	Recurrence	6 mo.	
29. Gubell. (footnote 32)	1928	?	?	Severe asthma	Left sympathectomy and partial vagotomy Double sympathectomy	2/21/	Unimproved	12 mo.	
						12/ 6/23	No attacks	32 mo.	

for bronchial asthma are recorded. Probably this gives us a more accurate conception of what can be expected from intervention on the extrinsic nerves. There are four rather extensive series in which nearly all of the patients have been followed for more than a year, and in some the earliest operations were performed five years previous to the report. Göbell,⁵² who had presented the most extensive series, had intended to wait until five years had elapsed since operation in his cases, but at the request of Lengemann summarized his results in June, 1928, in a symposium before the Association of Northwest German Surgeons. Although he had operated on 112 patients, he reported the results in only 98 of these. Consequently, though we do not know the average length of time the patients have been followed, it is seen that for a number of them the period of observation has been more than four years and that the ones operated on most recently have been excluded from consideration. Lengemann's⁵³ series, pre-

TABLE 4.—*Résumé of Results in Cases Included in Table 3*

Total Cases, 29		
Cure 8 cases, or 28 per cent Observed an average of 24 months	Improved 5 cases, or 17 per cent Observed an average of 15 months	Unimproved 16 cases, or 55 per cent Observed an average of 11 months
2 cases.....3 years or over	1 case.....2 years or over	7 cases.....1 year or over
2 cases.....2 years or over	1 case.....1 year or over	9 cases.....6 months or over
2 cases.....1 year or over	3 cases.....6 months or over	
2 cases.....6 months or over		

sented at the same meeting, is of particular merit in regard to the length of time elapsed since operation. He brought out the comparison between his results published in 1925 and those in the same cases two and a half years later. These two series furnish a fairly accurate history of patients who have undergone such operations. It is particularly disappointing that the two originators of the principal operations on the nerves, Kümmell and Kappis, have not seen fit as yet to give a careful statistical study of their results. Kümmell,⁵⁴ in the aforementioned symposium, made an impassioned appeal in favor of operation on the nerves. However, he contented himself with an elusive statement in regard to his results, to the effect that he had about 40 per cent cures and that a total of about 70 per cent of the patients operated on were improved. He made no statement as to the interval of observation. In 1924, Kappis⁵⁶ stated: "Of our patients operated with vagus division the large part after operation are freed from asthma . . . and only a few have not been improved." At that time, he stated that a sufficient number of patients had been operated on by sympathetic and vagus division to determine the value of these procedures by studying the

results after two or three years. In spite of a careful search, we have been unable to find any subsequent report on this subject from his clinic. In his discussion, Kümmell upbraided Kappis along with Fründ, Lengemann and others for expressing themselves less enthusiastically than three or four years previously. This is the only suggestion of a recent opinion by Kappis that we have found. If we had available a careful study of the results of Kümmell's and Kappis' operations

TABLE 5.—*Series Reported from Individual Clinics*

Reporter	Date	Total Cases	Total Operations	Operation	Number	Cured, per Cent	Improved, per Cent	Unimproved, per Cent	Unknown, per Cent	Mortality, per Cent	Interval
Göbell..... (footnote 52)	1928	98	105	Single sympathectomy	7	0	..	100	Uncertain; earliest operation 4½ years ago
				Double sympathectomy	19	42	11	42	5	..	
				Right vagotomy	1	0	..	100	
				One side sympathectomy plus vagotomy	16	50	..	19	21	..	
				Double sympathectomy with vagotomy	61	43	18	23	14	2	
				Total (by cases)	98	43	13	29	14	1	
Hesse..... (footnote 26)	1926	18	23	Unilateral sympathectomy, bilateral sympathectomy	18	28	17	56	Usually a year or so
Kaess..... (footnote 24)	1925	28	28	Unilateral sympathectomy	28	29	29	43	Over 6 months
Fründ..... (footnote 23)	1928	48	55	Sympathectomy	1	100	Not given; earliest case at least 3 years of age
				Vagotomy	47	13	21	66	
				Vagotomy and sympathectomy	7	100	
				Total (by cases)	48	12	21	67	
Lengemann (footnote 53)	1925	27	44	Unilateral sympathectomy	10	20	30	50	At least several months
				Bilateral sympathectomy	2	50	50	
				Vagotomy	3	33	..	66	
				Combined	12	33	33	25	
				Total (by cases)	27	33	26	37	..	1	
				Unilateral sympathectomy	11	18	..	82	
	1928	20	25	"	2	100	Over 2½ years
				"	2	50	..	50	
				"	10	10	20	70	
				Total (by cases)	20	15	15	70	
				Total five series	211	30	18	45	7	1	

during the years 1923 and 1924, our task of evaluating the procedures would be easier. The series recorded in table 5 give the results in 211 cases after a moderately long interval. While there is a variation from series to series in the exact proportion of (1) those who are symptom-free, (2) those who are improved, and (3) those who are unimproved, there is a surprising correspondence between the figures so obtained and those which we found by analysis in the cases reported in detail. Thus, of the 211 patients, 30 per cent are reported as cured; 18 per cent as improved; 45 per cent as unimproved and 7 per cent as unknown, with 1 per cent mortality. In no individual series is the

percentage of improved patients below 30 per cent. Summarizing the results reported in the literature, one finds that a few of the patients have had remarkable relief from a most serious asthmatic condition. About one third of the patients are completely relieved for the period of observation varying from six months to five years. Including these, about half of the patients have been definitely improved while half have been unimproved.

In selecting the cases for analysis, we have investigated all reported instances of such operations that we could find. We excluded a large number as unsatisfactory chiefly because a sufficient period of post-operative observation was not stated. In a few instances, we did not have access to the original articles (chiefly Russian). Leder⁵⁶ and Orth⁵⁷ mentioned the report of some other cases apparently given before local medical societies which were not included in the indexes of medical literature. The latter are included after the authors' names. The following is the list of these cases excluded from our statistical analysis.

- Bottner, two additional cases, *Med Klin* **21**:197, 1924
 Brschowski, three cases, *Nowy Chirurg Arch*, 1925 no 81
 Erkes, one case *Centralbl f Chir* **53**:718, 1926
 Ewojan, nine cases, no reference, quoted by Orth
 Fisban, one case no reference, quoted by Leder
 Flocken, four cases *Arch f klin Chir* **130**:68, 1924
 Frund, one case, *Beitr z klin Chir* **136**:58, 1926
 Von Genersich, one case, *Klin Wchnschr* **3**:2011, 1924
 Grekow, six cases, *Cong russe de chir*, 1925, quoted by Leder
 Heile, one case, *Centralbl f Chir* **51**:862, 1924
 Hesse, two additional cases, *Beitr f klin Chir* **136**:429, 1926
 Ischiyama, two cases, *Japan M World* **5**:289, 1925
 Jenckel, three cases, *Centralbl f Chir* **51**:897, 1924
 Jungmann and Bruning, three cases, *Klin Wchnschr* **3**:399, 1924
 Kappis, five cases, *Med Klin* **20**:1347, 1924
 Karditz, one case, no reference, quoted by Orth
 Kern, one case, *Surg Gynec Obst* **42**:28, 1926
 Kroll, three additional cases, *Deutsche med Wchnschr* **53**:1328, 1927
 Kummell, three cases, *Klin Wchnschr* **2**:1825, 1923
 Kummell, Jr, eight additional cases, *Beitr z klin Chir* **132**:249, 1924
 Lawen, one case, *Arztl Verein z Marburg Feb 21, 1924*, quoted by Leder
 Leriche and Fontaine, one additional case, *Bull et mem nat de chir* **54**:600 1928
 Lewit, six cases, *Cong russe de chir*, 1925, quoted by Leder
 Mandelbaum, eight cases, no references, quoted by Orth
 Mirizzi, one case, *Semana med* **1**:930, 1925
 Mravanadre, five cases, no reference, quoted by Orth
 Orth, two cases, *Vereinsbl d pfalz Aerzte* **5**:318, 1928
 Osoliy, two cases, no reference, quoted by Orth
 Neuber, one case, no reference, quoted by Leder
 Radice, three cases, *Ann ital di chir* **3**:9, 1924

Rehbein, one case, *Munchen med Wehnschr.* **72**:1885, 1925
 Rhode, one case, *Arch f klin. Chir* **139**:669, 1926
 Ringel, six cases, *Cong allemand de chir*, 1924; quoted by Leder.
 Popke, three cases, *Arch f klin Chir* **133**:148, 1924
 Rothfuchs, three cases, *Centralbl f Chir.* **51**:903, 1924
 Sauerbruch, two cases, *Arch f. klin. Chir* **133**:277, 1924.
 Schulze, two cases, no reference, quoted by Orth.
 Silberger, two cases, no reference, quoted by Orth
 Syjatuchin, two cases, no reference, quoted by Orth
 Winterwitz, one case, no reference, quoted by Leder.

Witzel,²⁸ in a footnote in 1925, spoke of forty cases but did not give details.

Bruning³⁷ mentioned twenty-six cases without details in the discussion of Kroll's report before the Berlin Surgical Society in 1927.

Kappis³⁶ spoke of vagotomy performed on a great many patients but has never even published the total number or given any detailed report of the results

In regard to the operation of choice, it seems to us that the statistical evidence is still too scanty for one to arrive at any final opinion. The patients in whom vagotomy alone was performed make the poorest showing of any large group. In fifty cases, 23 per cent have shown improvement. Without Kappis' results, it is difficult to decide on the value of this procedure. When used alone it seems to be less satisfactory than when combined with intervention on the sympathetic or than when the latter alone is done. The most favorable results reported in any extensive group are those of Gobell³². Curiously enough, the percentages of his symptom-free cases are practically the same (from 42 to 50) following (1) double sympathectomy, (2) unilateral sympathectomy plus vagotomy and (3) double sympathectomy plus vagotomy. Gobell concluded that unilateral sympathectomy is not followed by any lasting success. This certainly seems erroneous as some of the most brilliant results have followed unilateral sympathectomy; for example, three patients of Kummell's³⁵ who in 1927 had been symptom-free for three years and the two in Leriche and Fontaine's³⁵ 1928 report, relieved for two and a half and three years, respectively.

It is evident from studying some of the cases reported that a short interval of time is worthless as an index of the ultimate result. Frequently, a patient will improve for several weeks or months only to have a relapse. Case 12 from table 3 illustrates the fallacy of accepting as short a period of time as three months, as did Leder³⁶ in determining the result of operation. We have arbitrarily chosen six months as the minimum interval making the case worthy of study. In this analysis, we have stated as accurately as possible the interval following operation. Any one who chooses a longer interval for estimating results may do so from these statistics. We believe three years

at least should be the period of freedom following operation before we may speak of a cure of bronchial asthma. However, if at this time we took such a period there would be few cases available for analysis, though it is certain that several patients with bronchial asthma have been relieved for more than four years. A comparison of the two series of Lengemann⁵³ illustrates the danger of assuming a cure after a few months. But this equally demonstrates that even after another interval of more than two and a half years, 30 per cent of the patients still show improvement. Brüning's³³ position seems to us too conservative. As a matter of fact, his results as given in the discussion of Kroll's paper in 1927 correspond well with those obtained by other operators. At that time he stated that he would regard one third of his results as final cures if he had not seen relapses occur in many cases after a greater interval. It is possible that a relapse will occur in an occasional case after two or three years of freedom from symptoms, but we feel that this must be unusual.

REPORT OF CASE

Our interest in extrinsic nerve intervention in bronchial asthma was stimulated by the reports of Kümmell.²⁰ The case which we report here immediately suggested itself to us as a suitable one for attempted surgical relief. As the record shows, the patient had suffered from severe asthma for a number of years and was unrelieved by all of the usual types of medical treatment. He was found sensitive to more than fifty different proteins, and antiallergic measures were also unsuccessful. He was unable to work and spent long periods in the hospital. The fact that surgical intervention in the treatment of asthma was still in the experimental stage was explained to him, and after careful consideration he came to us asking for the operation.

We chose resection of the posterior pulmonary rami as the most logical operation. Section at this point interrupts the fibers controlling the finer air passages from both the vagus and the sympathetic including those crossing from the opposite side.

History.—W. T., a clothing cutter, aged 36, was admitted to the Rochester General Hospital on Aug. 23, 1928. The family and past histories were entirely negative for asthma or other allergic manifestations. He began having asthma in June, 1918, while serving in the United States Army at Kelly Field, Texas. Following a period of about seven weeks' hospitalization, he was discharged from the army for physical disability because of his asthma. Since that time, he has not been free from attacks for more than a week. The frequency and severity have progressively increased. About three years before admission, he had to stop work on account of them. He complained of shortness of breath at all times, worse when lying down. He was subject to frequent smothering spells and many nights sat up in a chair for hours at a time because of shortness of breath. He did not consider this severe enough to call it an attack of asthma. He had a chronic

productive cough with expectoration varying in amount from one half to two sputum cups daily. The sputum was bluish-gray, thick and nonodorous and had never contained blood. He frequently had had severe pain across the center of his chest, lasting three or four hours at a time, aggravated by cough or deep breathing. During an asthmatic paroxysm, he was conscious of a rapid heart action and had frequent sharp precordial pains. The weight had decreased from 195 to 156 pounds (88.5 to 70.8 Kg.). During the past five years he had been a regular attendant of the asthma clinic of the Rochester General Hospital and had been a patient in the wards of the hospital on numerous occasions, sometimes remaining as long as five months. His case was also studied at the Brooklyn Naval Hospital and at the United States Veterans' Bureau Diagnostic Center in Washington. In spite of all therapy the attacks of asthma increased in severity and frequency, and it became more and more difficult to secure relief by drugs during an attack. On Feb. 9, 1926, a tonsillectomy was performed. The removal of the tonsils had no effect on the asthma.

The severity of the asthmatic attacks and the seriousness of the disability can best be described by quoting a few abstracts from the hospital record of previous admissions. During a hospitalization period from Jan. 12, 1926, to June 17, 1926, it was necessary to use eighty-five doses of morphine ($\frac{1}{4}$ grain [16 mg.]) and 454 doses of codeine (1 grain [0.6 Gm.]) in addition to large amounts of epinephrine.

April 14, 1926: "For the last two days has been almost continuously in attacks, relieved only for a short time by epinephrine. Is getting large quantities of morphine and epinephrine with little relief. Ankles markedly edematous. Is a very sick man." "Since leaving the hospital on Dec. 1, 1926, has been improved but has had three or four attacks a week. Without epinephrine attacks last several hours or may run for a week at a time with eight to ten peaks of severity during the course of a day."

March 3, 1927: "Has been having a terrible time with asthma. Had nearly 100 minims (6.1 cc.) of epinephrine last night." "For the past one and a half months has had practically constant asthma, day and night, always worse at night. Coughing and expectorating a great deal."

Nov. 12, 1927: The patient was admitted to the hospital suffering from a severe attack of asthma. Medication the first night was as follows: 7:45 p. m., 15 minims (0.9 cc.) of epinephrine; 9:15, 15 minims of epinephrine; 12:27 $\frac{1}{100}$ grain morphine; 12:25, 15 minims of epinephrine; 12:27 $\frac{1}{100}$ grain (0.6 mg.) of scopolamine and $\frac{1}{100}$ grain glyceryl trinitrate; 12:30, amyl nitrite; 2:15, menthol inhalations. "Following this, patient slept until 5 a. m. when more epinephrine was necessary."

July, 1928: "Attacks very poorly controlled by epinephrine. Scopolamine more efficacious."

Physical Examination.—The patient weighed 70.8 Kg. (156 pounds) and was 181.5 cm. (5 feet 11½ inches) tall. The nose was normal. The tonsils had been removed. The fossae were clean. The thyroid showed no enlargement; the lateral lobes were barely palpable. The chest showed a drooping posture; the shoulders were rounded; the anteroposterior diameter was increased; the clavicles were raised anteriorly and were equally prominent. There was fair respiratory excursion, equal on the two sides. The percussion note was heard scattered throughout both lungs. The heart was not enlarged. The sounds were clear. There were no murmurs. The pulse rate was 78 when the patient was recumbent;

88 when he was sitting, and 88 when he was standing. The pulse was regular in rate and rhythm. The blood pressure was 116 systolic; 77 diastolic. The radial arteries were not sclerotic.

Laboratory Examinations.—Urinalysis was repeatedly negative. The blood showed white cells, 7,000; hemoglobin, 82 per cent; red blood cells, 4,464,000; differential polymorphonuclear neutrophils, 65 per cent; polymorphonuclear eosinophils, 8 per cent; lymphocytes, 32 per cent. The Wassermann reaction of the blood was repeatedly negative.

The blood chemical determination showed: nonprotein nitrogen, 35 mg. per hundred cubic centimeters; chlorides (whole blood), 510 mg. per hundred cubic centimeters; sugar, 120 mg. per hundred cubic centimeters. The sputum was repeatedly negative for tubercle bacilli. The electrocardiographic report showed a negative tracing. The vital capacity was 4,850 cc. (a 26 per cent increase over the normal for the patient's weight and height).

TABLE 6.—*Positive Reactions to Skin Tests*

Vegetables	Fruits	Epidermal Products
Asparagus	Peach	Chicken feathers
String beans	Apple	Goose feathers
Kidney beans	Grapefruit	Dog, hair and dander
Lima beans	Lemon	Horse, hair and dander
Navy beans	Orange	Rabbit, hair and dander
Irish potato	Watermelon	Cat, hair and dander
Sweet potato	Cantaloupe	Cow, hair and dander
Peas		
Beet		
Carrot	Grains	Beverages
Parsnips	Rye	Coffee
Turnip	Wheat leucosin	Tea
Cabbage	Barley	Cocou
Celery	Buckwheat	
Lettuce	Corn	Condiment
Onion	Oats	Black pepper
Spinach	Rice	Ginger
Egg plant		Mustard
Pumpkin	Meats	Paprika
Squash	Beef	Vanilla
Cucumber	Pork	
Tomato	Mutton	Special
Radish	Horse	Orris root
Swiss chard	Goat	Streptococcus (autogenous sputum)
Mushroom		
Okra		

Roentgen examination of the paranasal sinuses revealed some haziness of the right antrum. (It was later punctured and found normal.) Repeated examination of the chest on several admissions showed slight peribronchial infiltration but no evidence of tuberculosis. Roentgenograms of the chest taken during a severe asthmatic paroxysm revealed no essential difference from those taken during the interval between attacks.

The positive reactions to the skin tests for protein hypersensitivity are shown in table 6.

During the long period of observation of this patient, there was complete agreement that he was suffering from severe bronchial asthma. Skin tests demonstrated that he was sensitive to a large number of proteins. Although every possible precaution was taken to prevent his contact with these substances, there was no improvement in his condition. In the hope that his was a bacterial allergy, treatment was attempted by a vaccine made from streptococcus found in his sputum. This therapy gave negative results. The list of drugs used in the treatment of asthma was exhausted without benefit except for the alleviation of an asthmatic attack, and it was becoming increasingly difficult to secure relief

during a paroxysm. The patient stated that life was unbearable under these conditions. When he consulted us, all of the established medical measures had failed to stop the progression of the asthma. Consequently, we did not hesitate to suggest an operation still in its experimental stage.

Operation.—On Aug. 28, 1928, with the patient under gas-oxygen and novocaine hydrochloride anesthesia, we opened the right side of the chest widely under positive pressure obtained with the usual gas anesthesia apparatus. The scapula was mobilized by an incision encircling its angle. The fifth rib was resected from the transverse process to the anterior axillary line. The pleural incision was made through the bed of the fifth rib. The fourth rib was transected to increase the exposure. The lung was quite diffusely adherent to the parietal pleura but was easily separated by sharp dissection. When the lung was held forward, the right lateral wall of the mediastinum was easily reached. Our posterior incision gave excellent exposure. The azygos vein was taken as landmark. The vagus nerve was exposed by an incision through the mediastinal pleura above the vein. Novocaine hydrochloride was injected into the nerve. It was picked up on a hook and by the exertion of a little traction its location below the azygos vein was identified. Another incision was made through the pleura just below the vein, and the vagus was dissected downward, exposing four main branches running to the posterior surface of the bronchi (fig. 3). After these branches were dissected out to the parenchyma of the lung, they were cut. The main trunk of the vagus was entirely freed, insuring section of all the smaller branches. The vagus was cut at the inferior border of the right main bronchus, for fear there might be lower branches that had not been exposed. (We feel that section of the vagus trunk was an unnecessary step, and plan to omit it in the future.) Sympathetic fibers were not identified during the operation, but from our dissections and the observations of Braeucker we are sure that most of those going to the posterior pulmonary plexus were destroyed. The lung was made to expand fully and the chest wound closed in layers in the usual manner. The patient stood the operation well. Convalescence was delayed by a moderate sized hemopneumothorax which was gradually absorbed following aspiration.

Follow-Up Study Eight Months After Operation.—The patient was entirely free of asthmatic attacks for a period of three months following intervention. On Nov. 27, 1928, after spending several hours at an indoor circus he began to have some dyspnea. The patient is hypersensitive to horse dander. As there were many horses in the performance, it is probable that he received an overwhelming dose of this allergen. He was admitted to the hospital that evening with a typical attack of asthma. The medical resident noted that this attack was much milder than previous attacks in which he had seen him. Since that time he frequently has attacks of mild dyspnea, particularly at night, but the respiratory difficulty is not comparable to the severe asthmatic paroxysms that he had prior to operation. These attacks are controlled by a single dose of epinephrine, whereas previously he frequently required repeated doses, sometimes as much as 100 minims, in the course of a night. Narcotics are no longer required. He has complained of pain along the course of the incision and a feeling of tightness in the right side of the chest. He stated to one of the medical consultants that since his operation the attacks of asthma have been infinitely milder. Without our knowledge, he urged another patient with a severe form of asthma to have this operation performed.

SUGGESTIONS FOR FURTHER INVESTIGATION

The bronchostenosis producing the asthmatic attack being a bilateral reaction, the question naturally is raised as to how unilateral section of the extrinsic nerves can modify the paroxysm sufficiently to produce relief. The hypothesis advocated by several that the tonus in a supposed bronchoconstrictor center is diminished by the removal of unilateral afferent impulses does not impress us. The only explanation that is satisfactory to us has to do with vital capacity and air requirement.

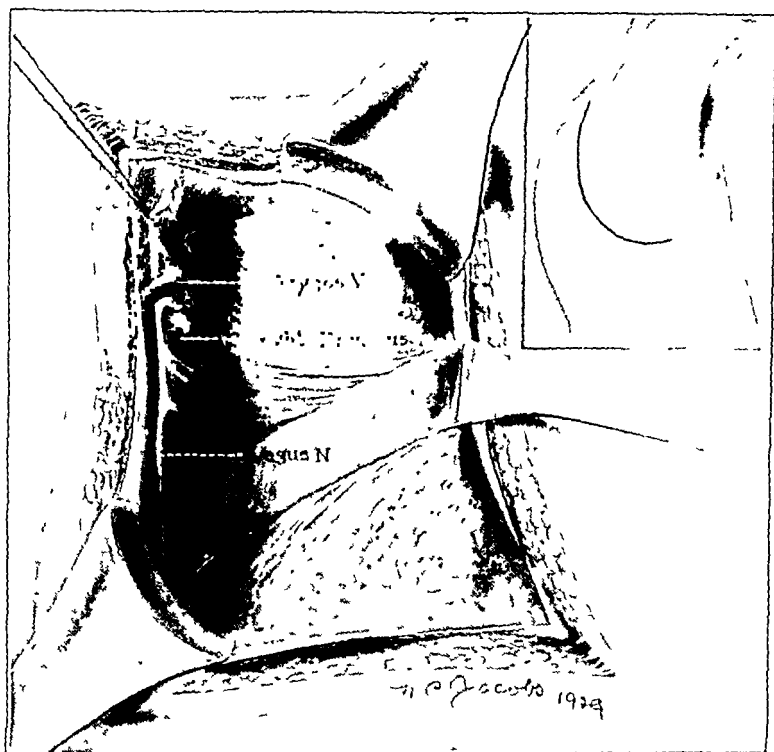


Fig 3—The operative exposure of the posterior pulmonary plexus through a posterior, transpleural incision.

Normal vital capacity is so much in excess of the tidal air that respiration can be carried on by one lung if its air interchange is free.

This conception affords a satisfactory explanation of the failures to relieve asthma. The continuation of a restricted air interchange on the side operated on may be due to: (1) an incomplete removal of the extrinsic nerve fibers to the lung (operation incomplete in plan or in technic) or (2) an uninfluenced thoracic cause (control by intrinsic nervous mechanism or rigid thorax). If the cause of a failure is the latter, no operation on the extrinsic nerves will avail. Intrathoracic

interruption of both vagus and sympathetic pathways to the lung is most likely to avoid the danger of the former cause. (In Kümmell's²⁰ two cases of posterior pulmonary plexus resection in which relief resulted, cervical sympathectomies had previously failed.)

We have briefly referred to roentgen therapy under the discussion of splenectomy. A few observers have published enthusiastic reports of this method of treatment (Schilling,⁵⁸ Gerber⁵⁹ and Klewitz⁶⁰). Freund²³ combined intervention on the extrinsic nerves with roentgen-treatment. At first, in 1926, he used the latter only in cases in which operation failed to relieve the condition. More recently, in 1928, he reported good results from roentgen therapy alone (70 per cent improvement). He advocated the trial of roentgen treatment before the consideration of operation. We feel that this position is sound if the therapy is not followed by unfortunate sequelae. Heavy dosage of deep roentgen therapy has sometimes caused fibrosis of the lung. It remains to be seen how much asthmatic patients can be benefited by roentgen treatment that is confined within this limit of safety. As Kümmell emphasized, whatever its value it is not to be considered ultimately as a competitor with extrinsic nerve operations because the latter are to be undertaken only after the failure of all conservative measures.

Entirely too little attention has been paid to the treatment of the fixed chest. It is universally recognized that emphysema and its accompanying chronic bronchitis are frequent complications of asthma. Most of the authors whose cases we reviewed stressed the presence of these conditions. Several of them went so far as to remark that the complete relief of dyspnea could not be expected on account of these complications even though the element of bronchostenosis should be entirely overcome by operation on the nerve. However, few undertook to correct the fixation of the chest. Many of these patients would probably have been greatly benefited by chondrectomy, and some of them relieved without operation on the nerve. (Compare Leriche's³⁶ fifth case, in which relief was obtained by chondrectomy plus sympathectomy plus vagotomy and in which the patient himself thought the chondrectomy was more beneficial than the operation on the nerves). In his experience, Ischiyama⁶¹ found mobilization of the wall of the chest of more value than cervical sympathectomy. We have discussed the various types of operations to overcome the fixation of the chest in the section headed "Operations for Bronchial Asthma." Chondrectomy (Freund) with destruction of the perichondrium has an excellent record of achievement. There is no other operation at present that seems to us as satisfactory for this purpose.

Bronchial asthma has been considered by many to be of psychogenic origin. The discovery of the allergic basis as a cause in many instances, at least, is definite proof of an underlying pathologic process. The

cure in isolated cases by simple measures involving the removal of a specific allergen from the patient's environment (such as chicken feathers or horse dander) would have been taken a few years ago as proof of the psychogenic basis for asthma. As the knowledge of this subject increases, one finds the explanation for more and more cases of asthma. Thus, there are separate groups susceptible to pollens, animal emanations, dietary constituents, bacterial proteins absorbed from infectious foci, etc. If asthma is a pure neurosis, the results of all operative procedures should be identical. However, we have seen that after operations on the nose and throat practically no lasting improvement of the asthma follows, while operations on the extrinsic nerves of the lung have given a fair percentage of completely relieved patients. There is a psychogenic factor in all diseases, and from this the asthmatic patient is not immune. Probably it is greater in such patients than it is in cases of ruptured duodenal ulcer, but this factor does not completely explain the pathogenesis in one any more than in the other.

Pathologic changes in the sympathetic ganglions removed at operation from asthmatic patients have been described in the literature, consisting of degeneration, fatty changes, scarring, chronic inflammatory reaction, etc. However, these are not specific for asthma. A correlation of any gross or histologic nerve lesion with a definite clinical syndrome would be of much interest but has not yet been achieved. This subject deserves further pathologic study.

Some method of choosing in advance those patients who will be benefited by operations on the nerves would be extremely valuable. Rehbein⁶² spoke of tenderness over certain cervical sympathetic ganglions and asserted that the removal of the latter alone is followed by the relief of asthma. It seems to us extremely unlikely that this point will prove to be an important aid in the selection of cases. The temporary interruption of nerve paths may be a much more useful test. Rehbein noted at operation that in the successful cases local infiltration with procaine hydrochloride caused freer breathing and subjective improvement even before the incision was made. Dramatic relief of extreme dyspnea at the moment that the vagus nerve was anesthetized was obtained in the fifth case of Leriche and Fontaine³⁶. They, as well as several others, have suggested a preliminary blocking of the autonomic nerves during an asthmatic attack. If this affords the patient relief, they advise operative intervention on the nervous system. This seems like a reasonable test, and it should be given careful trial. It appears to us less likely that it will assist those who interrupt only one system to decide between vagus section and sympathectomy.

CONCLUSIONS

1. Although our knowledge of the mechanism involved in producing the asthmatic attack is most incomplete, the hypothesis that the extrinsic nerve supply of the lung plays a significant rôle in it is the basis of operative interventions on the autonomic nervous system.

2. Anatomicophysiological studies indicate that there is a bilateral, bisystem nervous control of the size of the lumen in the finer air passages.

3. More than 300 operations on the autonomic nervous system in the treatment of bronchial asthma have been reported. Many of these are inconclusive for lack of sufficient data. An analysis of the carefully followed and reported cases showed that: (a) in about one-half, the operations have been complete failures; (b) in the others, varying degrees of improvement have been obtained, and (c) there have been a few brilliant cures in apparently hopeless cases.

4. Successful results have followed interruption of the vagus alone as well as of the sympathetic system alone. When operation on one system has failed, the interruption of the other is less commonly successful. However, the initial severing of both systems at the posterior pulmonary plexus seems to us the most logical intervention. An insufficient number of patients have been operated on in this manner to determine its comparative value. We report one case in which benefit was obtained over a period of eight months by this procedure.

5. Intervention on the autonomic nervous system for asthma should be considered as being in the experimental stage. However, if no contraindications are present, the results empirically obtained in this manner justify the attempt to relieve severe paroxysmal asthma when conservative measures, especially antiallergic methods, have without avail exhausted their possibilities.

6. Many asthmatic patients have a sufficient degree of emphysema and fixation of the thorax greatly to limit the respiratory exchange. In such cases, if the cardiac function is not already too greatly impaired, a mobilizing operation should be performed on the thoracic wall. This procedure alone may afford great relief from the asthma and should at least precede any operation on the autonomic nervous system in such instances.

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DECORTICATION OF THE HEART (DELORME) FOR ADHESIVE PERICARDITIS

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Cases of adhesive pericarditis in which the patients are amenable to operative treatment may be divided somewhat arbitrarily into two groups. The commonly recognized form of the disease is that in which the mediastinal adhesions binding the pericardium to the wall of the chest dominate the picture. In other cases, however, the contraction of the thickened pericardium itself produces cardiac failure by interfering with the proper action of the heart. The recognition of the two types of the disease is of prime importance when surgical intervention is considered. It becomes obvious that no single operative procedure can be effective when the differences in the morbid anatomy are considered.

The term *mediastinopericarditis* is properly applied to that form of the disease in which a firm cicatrix in the anterior mediastinum binds the outer aspect of the pericardium to the wall of the chest. The systolic contraction of the heart is hindered, as in every contraction the cardiac muscle must meet and overcome the resistance of the rigid bony framework of the thorax. The cardiac decompensation occurring under such circumstances is attributed to the strain which this abnormal fixation to the wall of the chest throws on the heart—an organ which has already suffered myocardial damage from infection. It is not improbable that the distortion caused by the fixation of the heart during respiratory movements may also produce a relative valvular insufficiency. A positive diagnosis is more frequently made in this type of the disease, and the patient is not uncommonly referred for surgical treatment. The systolic retraction of the wall of the chest gives a strong and readily understood indication for cardiolysis.

In operating for this condition one aims to free the heart from the unyielding scar which binds it to the wall of the chest. This is readily accomplished by the removal of the cartilaginous or bony portion of the ribs overlying the heart. Such an operation is the cardiolysis of Brauer or, more correctly, *thoracolysis praecardiaca*, a term suggested by Kocher.

In the second type of adhesive pericarditis, the heart is found encased in a veritable coat of mail formed by a thickened and inelastic pericardium. In these cases of *concretio pericardii* the heart becomes so throttled by the unyielding wall of scar tissue that its chambers can no longer expand in diastole to receive the inflowing blood. A marked

degree of stasis is produced in the veins, particularly the inferior caval system. The action of such a heart has been compared by Rehn to the restricted movements of a hand in a tightly fitting glove.

As a matter of fact, all degrees of transition exist between the two types, and Volhard,¹ who has submitted an excellent description of the clinical picture of concretio pericardii, expressed the feeling that the difference lies more in the degree of contraction than in the type of adhesion.

Patients in the first named group with adhesions between the pericardium and the anterior wall of the chest may progress until they show a more or less high degree of decompensation with the classic signs and symptoms of cardiac passive congestion. In addition, there is present the characteristic retraction of the precordial area of the wall of the breast with every systole and a bulging back during diastole. The presence of a marked thrill of the thoracic wall indicates a still powerful heart action and a competent diastolic filling of the chambers. On the other hand, when the heart is throttled by a contracted pericardium, the clinical picture is characterized by a striking disproportion between the high degree of cardiac passive congestive symptoms and the slight objective cardiac signs. In the words of Volhard: ¹

We find all that belongs to the general picture of marked cardiac decompensation—edema, effusions in the body cavities, liver swelling, dyspnoea on exertion, incapacity for work, but we fail to find the signs in the heart that we are accustomed to associate with such a condition and that account for the symptoms. We find no widening, rather a small heart; no apex impulse; no thrill of the chest wall; usually pure but strikingly soft sounds. *The unfavorable diastolic filling of the heart produces a small, weak pulse, often smaller with inspiration.* By fluoroscopy the heart appears to stand still, so slight are the evidences of heart motion. Very important but not peculiarly specific and present in both types is the lack of elevation of the anterior wall of the chest in breathing that Wenckebach has demonstrated.

But the finding that particularly indicates a seriously impeded diastole is the marked distention of the cervical veins, that do not empty in the upright posture, and especially in the upright position show a very characteristic double collapse in systole and diastole.

Moritz-Tabora measured the venous pressure in the arm veins and found very high values of 200 to 300 mm. of water. This accounts for a marked degree of liver congestion and the tendency to hydrothorax and early ascites, even before edema of the legs supervenes.

These "ascites praecox" can for years be subjected to countless tapings, unnecessary exploratory laparatomies, Talma operations, and false diagnoses.

The most striking single characteristic of the picture is marked venous stasis with a small heart. It is impossible to conceive of a

1. Volhard and Schmieden: Klin. Wchnschr., 1923, no. 1, p. 5.

distensible right auricle and ventricle remaining undilated in the presence of such a high degree of venous stasis—and it is exactly this lack of overfilling of the right side of the heart that led Volhard to employ the term "Einfluss stauung" or "inflow stasis." In the treatment of a patient in this type of case it is clear that there is nothing to be expected from the removal of the bony wall of the chest. Nothing less than a deliverance of the heart from its cicatricial coat of mail can influence the course of the disease.

Before discussing the literature which bears on the subject of decortication of the heart, an account of a case in which the operation was successfully performed will be presented. The patient was referred to me by Dr. Paul D. White to whom I am indebted for the diagnosis and medical care of the patient.

REPORT OF CASE

History.—C. S. was an American school girl, aged 18. At the age of 5 the patient was troubled by occasional spells of dyspnea, and her physician said that she had an enlarged liver and ascites. When 14 years of age, she had a succession of peritonsillar abscesses which were accompanied by attacks of dyspnea on exertion and "smothering spells." Again she was told that she had ascites.

First Admission.—On Jan. 26, 1925, at the age of 15, she was admitted to the medical service of the Massachusetts General Hospital, where a diagnosis was made of chronic adhesive pericarditis, perihepatitis, ascites and chronic tonsillitis. The patient showed no respiratory distress. The entire right hemithorax moved with each heart beat. The heart itself was enlarged, the apex impulse being in the fifth interspace, 8.5 cm. to the left of the midsternal line. The apex impulse shifted with change in position. There was no Broadbent's sign. A well defined systolic murmur was heard about the apex transmitted to the axilla. No diastolic murmurs were heard. The heart sounds were of good quality and regular with a third sound at the apex. There was no evidence of pulmonary congestion, but the liver was enlarged, the edge extending 6 cm. below the costal margin. There was a moderate degree of ascites. The cervical veins were slightly engorged and pulsating. Digitalis produced no definite change in the condition of the heart.

Second Admission.—On June 19, 1925, the patient was readmitted to the Medical Service. In the interval she had had her tonsils removed. As there was a definite increase in the ascites, 4,500 cc. of pale fluid was withdrawn by abdominal paracentesis. Inoculation into a guinea-pig gave negative results. The total protein content of the abdominal fluid was 4.8 per cent; that of the plasma was 6.4 per cent. An electrocardiogram showed slight left axis deviation. The vital capacity was 2,600 cc. She remained on the medical wards for one month on treatment with diuretics without effect.

On Aug. 18, 1927, she was seen in the cardiac clinic of the outpatient department. Two months after discharge from the hospital, 10 quarts of abdominal fluid had been removed by her physician. Her activities had been restricted during the two year interval but not entirely. She had been able to walk and to climb stairs. Edema of the legs had appeared within the past month. Examination of the heart now showed the apex impulse fixed in position. A few moist râles were heard at the left base, and there was definite ascites. She was advised to go home, remain in bed, and take digitalis and theophylline, U. S. P. (theocin).

Three weeks later it was noted that there was still well marked edema of the shins which had not disappeared with the digitalization.

On April 26, 1928, the following note was made in the cardiac clinic: "Doing poorly. In bed a good bit of the time throughout the winter. Legs and abdominal wall edematous. Abdomen tapped in February. Takes no digitalis. Had theocin a month ago without effect. Physical examination as before except for cyanosis which is now present."

At this time, the following letter was written by Dr. Paul White to her physician: "Yesterday morning in the Cardiac Clinic here, I saw C. S. again and found her in poor condition. She certainly has had a very miserable time and I am afraid there is not much can be done to help her. There seems little doubt that pericarditis must be at the back of her trouble. Probably she has a good deal of mediastinal involvement and disability of the heart itself. . . . I would suggest resuming digitalis $1\frac{1}{2}$ grains once daily for a few days, then once daily for two weeks. If after two or three weeks she is not better I would suggest that she come to the hospital again with the thought to consider cardiolysis, in case there is any chance of freeing the heart of some of the extra work that it is doing. I suppose, however, that the prognosis is rather poor at the best."

Third Admission.—The patient entered the Massachusetts General Hospital for the third time on June 8, 1928. For the past month she had been confined to bed and was orthopneic. She was dyspneic on slight exertion, and the edema of her lower extremities had markedly increased. On physical examination the heart seemed fixed in position, and in addition to the observations already noted a pulsus paradoxus was observed. Signs of fluid were found at both bases. There was extreme edema of the lower extremities extending upward over the sacrum. The vital capacity was 1,600 cc. as compared with 2,600 cc. three years before. Roentgen examination showed dulness of both bases obliterating the outlines of the diaphragm, rising to the level of the fourth rib on the right. The heart shadow appeared large and prominent in the region of the left ventricle. From the lateral aspect the sternum seemed to move normally away from the mediastinal shadow on deep inspiration. There appeared to be no adhesions between the sternum and the mediastinum. There was considerable increase in the dulness in the right cardiophrenic angle with some limitation of diaphragmatic excursion in this region. She was given an organic mercury compound in repeated doses, but the slight diuresis caused only a transient loss of weight. On July 16, 2,500 cc. of clear fluid was removed from the abdomen.

In considering the case of C. S. with a view to planning operative relief, it was felt from the outset that nothing was to be gained by the Brauer operation. It is true that three years before, the cardiac pulsations were described as being forcefully transmitted to the wall of the chest and the heart appeared to be enlarged. A definite systolic retraction of the ribs and interspaces had never been observed, however, and now, in contrast, the heart seemed small, particularly in relation to the high degree of venous stasis. The pulsations were but feebly transmitted to the wall of the chest, and the sounds were distant and muffled. Roentgen examination failed to show evidence of adhesions between the pericardium and the anterior wall of the chest. The signs and symptoms seemed clearly to be those of the "inflow stasis"

or impeded diastolic filling so vividly described by Volhard and Schmieden.¹

Certain physiologic considerations have more than a mere theoretical bearing in planning the operation of decortication of the heart. The unfortunate results in several of the cases of pericardial resection that have found their way into the literature have emphasized the importance of having clearly in mind an accurate knowledge of the pathologic changes in the individual case. Schmieden² has given a helpful analysis of the causes of the successes and failures in his series of seven cases.

At the outset, one is forced to admit that no reliable criteria exist for determining the capability of the cardiac musculature to withstand the suddenly increased load. Numerous observations and experiments³ have demonstrated that under the conditions of normal life the pericardium plays no important part in supporting the wall of the heart. Conditions may be different, however, when the myocardium has been damaged by infection. Further, in an individual case it may be difficult to differentiate the symptoms of cardiac failure due to mechanical factors from those referable to myocardial weakness. If improvement results from digitalis therapy, it is probable that the myocardial insufficiency is playing an important rôle in the case under question. If improvement does not follow rest and the administration of digitalis, the mechanical factors may be considered paramount, but an underlying myocardial weakness cannot be excluded.

Of equal importance to the state of the myocardium and a point concerning which one may more readily inform oneself is the matter of the balance between the action of the right and left ventricles. It is of the greatest importance to ascertain the extent to which the scar involves these two chambers. If the output of the right ventricle is suddenly increased by decortication while the left ventricle remains encased in scar, the area of venous stasis is merely transferred from the caval systems to the lungs, and disaster follows. This very happening has undoubtedly been responsible for some of the deaths on the operating table. If the left side of the heart is involved in the scar, it must be liberated before freeing the right chambers. Schmieden² now advises a transpleural approach for this purpose.

Fluoroscopic examination in different positions with special observation of the movements of the ventricles is invaluable in ascertaining the extent to which each is involved in the scar. Other signs of

2. Schmieden, V., and Fischer, H.: *Ergebnisse des Chirurgie u. Orthopädie* 19:98, 1926.

3. Beck, C. S., and Moore, R. L.: *The Significance of the Pericardium in Relation to Surgery of the Heart*, *Arch. Surg.* 11:550 (Oct.) 1925. Grant, R. T.: *Heart* 13:371, 1926.

encasement of the left side of the heart are effusions in the pleural cavities, stasis in the pulmonary circuit and a widening of the cardiac shadow to the right.

In the patient under consideration, fluoroscopy showed the heart shadow to be large and prominent in the region of the left ventricle. Further, the lack of improvement with digitalis gave evidence that the apparent cardiac failure might fairly be attributed to purely mechanical factors. Operation was proposed therefore, for the release of the right ventricle by resection of the adherent pericardium.

Operation.—On July 18, 1928, with the patient under ether anesthesia, an incision was made extending along the line of the second rib to the middle of the sternum, bearing directly downward to the xiphoid, then laterally along the seventh costal cartilage (fig. 1). The skin flap so outlined was reflected outward with the pectoralis muscle. The cartilages of the third, fourth, fifth, sixth and seventh

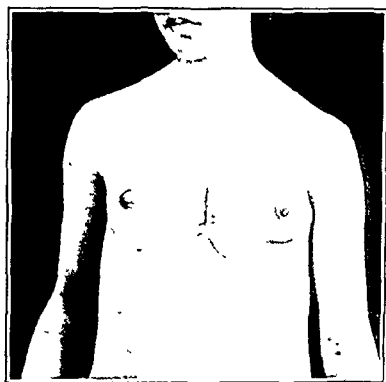


Fig. 1.—Incision three weeks after the operation.

ribs were resected, taking in addition 1 inch of the bone of the fourth and fifth ribs, respectively (fig. 2). The internal mammary vessels were ligated in the second interspace, and the intercostal muscles with the posterior layer of the perichondrium of the costal cartilages were removed. The left pleural reflection was retracted laterally by blunt dissection. The anterior surface of the pericardium appeared as a firm white scar which did not transmit the pulsations of the underlying heart. An incision was made through the pericardium which was found to be 1.5 mm. in thickness. When the left ventricle was reached, the pericardium was carefully separated from the surface of the heart, the dissection being carried medially over the right ventricle. The adhesions between the visceral and parietal surfaces of the pericardium were in the main separated by the finger without causing any bleeding. In a few places over the right ventricle scissor dissection was used. The pericardium was removed in small fragments as it was freed. In the end there was a defect as large as the palm of one's hand, the heart herniating through this opening as though making ready use of the space which had been made available (fig. 3). The left half of the sternum was removed with rongeurs, and the dissection of the pericardium was carried as far as the auricle. The heart was then raised and separated from



Fig. 2.—Resected portions of third to seventh costal cartilages and rib ends.

the diaphragmatic pericardium until the vena cava could be seen. The diaphragmatic pericardium was much thickened and was contracted in one place into a *strong fibrous band*, 8 mm. in diameter, which seemed to rest in the angle between the inferior vena cava and the right auricle like a sling (fig. 4). This band was studded with calcareous deposits and was attached anteriorly to the surface of the diaphragm in the region of the xiphoid. It was resected by a V-shaped incision the apex of which lay at the vena cava. Following this, the edges of the pericardium retracted and revealed the musculature of the diaphragm beneath. Adhesions about the apex of the heart were loosened, but attention was chiefly directed to the right side of the heart and the diaphragmatic pericardium. The reflection of the right pleura was stripped back by blunt dissection, neither pleural cavity being entered. At the conclusion of the operation the skin

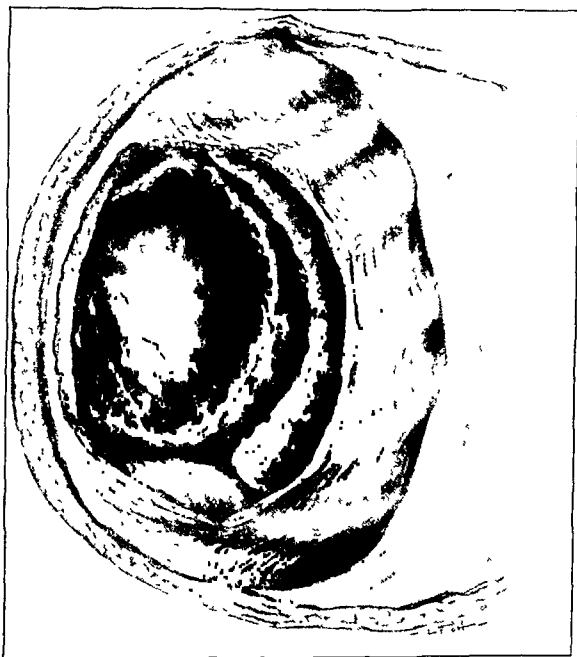


Fig. 3.—Window in the thickened pericardium being created by resection.

and muscle flaps were turned back into position, leaving the surface of the heart in direct contact with the under surface of the pectoralis muscle. The apex impulse was now transmitted forcefully through the tissues of the breast. For a time during the freeing of the adhesions about the vena cava adequate exposure necessitated pressing on the right side of the heart with the flat surface of the hand. This distinctly interfered with the filling of the heart, and the anesthetist reported that the blood pressure could not be obtained. Conditions returned to normal, however, when the hand was removed. The patient left the table in excellent condition. Convalescence was without notable incident. The edema of the extremities rapidly subsided, less edema being present in the legs ten days after the operation than at any time during the preceding year. Diuresis was evident in the relation of the fluid output to fluid intake, the most notable degree occurring on the fifth day postoperatively.

On August 7, the patient was allowed to sit up in a chair. There were no ill effects. She had lost 20 pounds (9 Kg.) of weight, most of which, of course, was accounted for by the disappearing edema. Her strength rapidly increased, and on August 16, one month after the operation, she was discharged from the hospital.

On September 7, seven weeks after the operation, she reported at the cardiac clinic and was found to have no edema of the feet or legs. The enlarged liver was still palpable 6 cm. below the costal margin, but there was no ascites. Improvement continued to be rapid, and she was advised to increase her activities.

On March 7, 1929, she was found to be in excellent spirits and had gained considerably in weight and strength during the winter. She was able to walk



Fig. 4.—Further stage in pericardial resection showing the elevation of the heart and freeing of diaphragmatic pericardium. The bandlike elevation is shown extending backward toward the inferior vena cava. This band was resected with the adjacent scar.

four miles a day without any shortness of breath. In coming to the clinic she said that she had run a considerable distance to catch the train. There is now no edema, and the abdomen shows no evidence of ascites. The pulsation of the heart is palpable as a forceful thrust in the window to the left of the sternum.

On Aug. 27, 1929, a report from Dr. Paul D. White referred to the patient as being in a "splendid" condition.

The question of reformation of the adhesions in this case must be left for the future to settle. In the cases reported in the literature such an occurrence has not been found to be a real danger, the usual course

being one of continued and progressive improvement. It has been suggested on the basis of experimental work that the pericardial defect be repaired with a fat or fascia transplant.⁴ I agree with Schmieden's policy of not adding a procedure of this nature to the operation unless further clinical experience makes it seem imperative.

REVIEW OF LITERATURE

Weill,⁵ in 1895, recognized that the rational treatment of this type of adhesive pericarditis lay within the purview of surgery. This view was expressed in the following words:

Lorsque la symphyse est arrivée au stade fibreux, elle est complètement émancipée de sa cause, et les moyens médicaux sont illusoires. On n'a jamais songé à faire de débridement dans ce cas, moins peut-être par résignation, que par incertitude du diagnostic. Il y aurait lieu de faire une tentative de ce genre, qui consisterait à libérer une partie du coeur, la point par exemple et la face antérieure. . . . C'est à la chirurgie qu'il appartiendra un jour de délivrer le coeur de la coque qui l'étrangle.

(After the adhesions have reached a fibrous stage, they act independently of their original cause, and medical therapy is illusory. One has never dreamed of attempting a débridement in such a case, less perhaps from resignation than from the uncertainty of diagnosis. There would be good cause to make an attempt of this kind, designed to liberate a part of the heart, the apex for example, and the anterior surface. . . . It will one day come within the province of surgery to deliver the heart from the shell which strangles it.)

Three years later (1898), the operation of decortication of the lung gave Delorme⁶ the idea that the same principles could be applied to a heart encased in an adherent pericardium. Detailed observations were made on cadavers, and it was found that adhesions between the heart and pericardium could be freed either with the scissors or bluntly with the finger. The operation of Delorme is not infrequently referred to as a lysis of intrapericardial adhesions followed by closure of the pericardium. As a matter of fact, Delorme recommended an actual excision of a portion of the pericardium in suitable cases. Further, when the adhesions are found to be too closely adherent to permit of a separation, he advised a section of the pericardium at its diaphragmatic attachment anteriorly.

Delorme⁷ plead for the adoption of his proposed operation in numerous communications addressed to the clinical societies of Paris. His

4. Klose, H.: Arch. f. klin. Chir. **117**:138, 1921.

5. Weill, E.: *Traité des maladies du coeur chez les enfants*, Paris, 1895, p. 128.

6. Delorme, E.: Gaz. d. hôp., 1898, p. 1150.

7. Delorme, Edmond: Bull. et mém. Soc. de chir. de Paris **24**:918 (Oct.) 1898; Soc. méd. d. hôp. de Paris, 3 series **37**:318, 1914; Gaz. d. hôp. **86**:2269 (Dec. 16) 1913; *ibid.* **87**:341 (Feb.) 1914.

proposals met with slight favor, however, and in 1902 the simpler procedure designed by Brauer⁸ was announced from Germany. Cardiolytic by the simple resection of ribs and costal cartilages gained popularity, and the theoretical principles so carefully worked out by Delorme were discarded as being too unnecessarily hazardous for clinical application.

Carl Beck, speaking before the American Medical Association in 1901,⁹ briefly referred to the possibilities of surgical relief in adherent pericarditis.

Rehn¹⁰ is commonly accredited with pointing the way toward the practical application of the theories of Delorme, and was the first operator to report the results in cases in which an excision of a portion of the pericardium had been carried out. It is to be noted, however, that Sauerbruch¹¹ as early as 1913 had freed the heart and resected a portion of the pericardium in a patient who had been confined to bed by dyspnea and who showed general edema. The patient was reported as being symptom-free and able to work eleven years after the operation.

In 1913, Rehn¹² expressed himself as being doubtful whether a heart which is encased in scarred tissue could be freed. He considered the intrapericardial lysis of adhesions to be impracticable because of the rapid reformation of new adhesions. As a matter of fact, this very thing had happened to mar the good result which he had obtained in a child. In a later communication, Rehn¹³ reported the results of extensive studies in the pathologic physiology of the various types of adhesive pericarditis. He then clearly described the technic and application of pericardial resection which he had carried out in four cases.

Case reports of successful operations have appeared with increasing frequency, particularly from Germany. Schmieden² has had a more extended experience than any other single operator, and I have already referred to his admirable analysis of the physiologic mechanisms involved in the operation.

The reported operations or attempts at operation have been listed in the accompanying table. In all, there have been collected the data in thirty-seven cases in which an operation was performed, five (cases 8, 9, 10, 11, 31) of which were interrupted. The deaths directly attributable to the operative procedure number seven (cases 6, 7, 12, 14, 19,

8. Brauer, L.: *Arch. f. klin. Chir.* **71**:258, 1903-1904; *München. med. Wchnschr.* **49**:1072, 1902.

9. Beck, Carl, in discussion on Norbury, F. P.: *Some Points in the Treatment of Pericarditis*, *J. A. M. A.* **37**:1585 (Dec. 14) 1901.

10. Rehn, L.: *Berl. klin. Wchnschr.*, 1913, p. 241; *Arch. f. klin. Chir.* **102**:1, 1914; *Med. Klin.* **16**:999, 1920.

11. Sauerbruch, Ferdinand: *Die Chirurgie der Brustorgane*, Berlin, 1925, vol. 2, p. 298.

12. Rehn (footnote 10, first reference).

13. Rehn (footnote 10, third reference).

*Results of Operation in Thirty-Seven Cases Reported in the Literature **

Case	Author	Operator	Age	Sex	Result
1	Rehn ¹¹	Rehn			Primary result good benefit not lasting because lesion was tuberculous
2	Rehn, ¹² Picard (Med klin 10: 271, 1923)	Rehn	6	♀	Primary result good, benefit not lasting because lesion was tuberculous
3	Rehn ¹³	Rehn	13	♀	Excellent, died later due to recurrence of rheumatic fever
4	Rehn ¹³	Rehn	14	♂	Excellent, died 1½ years later of influenza
5	Sauerbruch ¹¹	Sauerbruch	23	♂	Complete relief of symptoms 11 years after operation
6	Sauerbruch ¹¹	Sauerbruch	21	♂	Died 18 days after operation of cardiac insufficiency
7	Sauerbruch ¹¹	Sauerbruch	23	♀	Died 21 hours after operation of exhaustion
8	Sauerbruch ¹¹	Sauerbruch	30	♂	Operation interrupted because of cardiac irregularity good result nevertheless, died 4 years later of renal tuberculosis
9	Volhard and Schmieden ¹	Henle			Attempt abandoned because of tearing right ventricle
10	Volhard and Schmieden ¹	Heuck			Attempt abandoned because of tearing right ventricle
11	Volhard and Schmieden ¹	Brauer			Attempt abandoned because of tearing right ventricle
12	Volhard and Schmieden ¹	Voelcker		♀	Weak girl, died soon after operation
13	Volhard and Schmieden ¹	Voelcker		♂	Young man died 14 days after operation of severe tuberculosis
14	Volhard and Schmieden ¹	Voelcker			Incomplete removal, died, autopsy showed unyielding scar still encasing the heart
15	Volhard and Schmieden ¹ Schmieden and Fischer ²	Schmieden	30	♂	Two operations (1) small section of pericardium removed from right ventricle, temporary relief (2) transpleural decortication of left ventricle symptomatic cure 4 years after operation
16	Volhard and Schmieden ¹ Schmieden and Fischer ² Schmieden (Munchen med Wchnschr 69: 177, 1922)	Schmieden	46	♂	Complete relief of symptoms
17	Schmieden (Zentralbl f chir 51: 46, 1924) Schmieden and Fischer ²	Schmieden	22	♂	Temporary improvement died 3 weeks later autopsy showed extensive involvement of cardiac muscle
18	Schmieden and Fischer ²	Schmieden	18	♂	Complete relief of symptoms
19	Schmieden and Fischer ²	Schmieden	18	♂	Died on table at end of complete operation from dilatation of right heart
20	Schmieden and Fischer ²	Schmieden			No particulars concerning sixth case of Schmieden's series, listed as "improved"
21	Schmieden and Fischer ²	Schmieden	5	♂	Postoperative course complicated by extensive wound infection pneumonia and empyema improved
22	Bittröf (Munchen med Wchnschr 71: 517, 1924)		18	♀	Improved markedly, Talma operation performed later
23	Délagnerie (Gaz d hop 86: 1033 [June 5] 1913)		28	♀	Relief of symptoms not definitely stated that pericardium was resected
24	Guleke and Lommel (Klin Wchnschr 4: 737, 1925)		27	♂	Excellent result venous pressure reduced from 165 mm to 42 mm
25	Kirschner and Matthes (Deutsche med Wchnschr 52: 221, 1926)		22	♂	Excellent result 2 months after operation
26	Koennecke (Munchen med Wchnschr 51: 100, 1925)		21	♂	No improvement, advancing cachexia attributed to hepatic insufficiency
27	"		9	♂	Excellent result
28	"	Sattler	20	♂	Excellent result
29	Ljungdahl and Tengwall (Acta chir Scandinav 59: 480, 1923)		46	♂	Complete relief of symptoms 2 years after operation
30	Enderlen (Zentralbl f chir, 1925, p 589) Sauerbruch ¹¹	Enderlen	19	♂	Improvement for 3 months recurrence of symptoms with death

* A case report referred to by Guleke (Mitt a d Grenzgeb d Med u Chir 40: 23, 1927) but which has not been available is that of Tilmanns in which the patient is said to have died of recurrence of symptoms in nine months. Minkin (Vestnik Khir 10: 52, 1927) is also said to have reported a case of pericardial resection.

† In this column, ♂ indicates male, and ♀, female.

*Results of Operation in Thirty-Seven Cases Reported in the
Literature—Continued*

Case	Author	Operator	Age	Sex	Result
31	Lilienthal (Thoracic Surgery, 1925, vol 1, p 422) Loesen and Kahl (Zentralbl f Chr 51:2385, 1924)	Lilienthal	31	♀	Right auricle torn in attempting separation; operation abandoned; slow recovery
32	Hanebuth and Naegeli (Med Klin 23:1253, 1927)			♂	Died of cardiac insufficiency 1 hour after operation
33	Lauen and Matthes (Deutsche med Wchnschr 54:617, 1928)		21	♀	Improved
34	Cutler and Beck (Nelson's Loose-Leaf Living Surgery, vol 4)	Cutler			Died 1 hour after operation from myocardial failure
35	Churchill	Churchill	16	♀	Complete relief of symptoms 14 months after operation
36	Delorme (Progres med, 1924, p 457); Hallopeau (Bull et mem Soc nat de chir, 1921, T. 47, p 1120)	Hallopeau	16	♀	Operation performed during search for encapsulated rheumatic effusion which was not found, complete relief of symptoms
37	Delorme (Progres med, 1924, p 457); Hallopeau (Bull Soc de pediat de Paris, 1923, T. 21, p 206)	Hallopeau	7	♂	Accompanied by acute osteomyelitis of femur; pericardium resutured, recovery

32, 34) or 21.8 per cent of the cases in which operation was completed; two patients (cases 13, 26) showed no improvement (6.2 per cent); the improvement was transitory, and the patient died of the original disease in four cases (1, 2, 17, 30), or 12 per cent; in the nineteen remaining cases (59 per cent), the result was excellent, and frequently there was almost complete relief from symptoms. Three of the patients in the latter group died of intercurrent disease.

SENSIBILITY OF THE EXPOSED HUMAN HEART AND PERICARDIUM *

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Knowledge of cardiac and pericardial sensibility, as we have found it presented in published reports, is meager and incomplete. There is little agreement among the reporters as to the facts. This is largely due, we believe, to the scarcity of opportunity for careful observation on the open pericardial cavity of patients who are neither narcotized, shocked nor very toxic.

We recently availed ourselves of an unusual opportunity to investigate extensively the sensory reactions of the exposed human heart and pericardium to various forms of stimulation.

REPORT OF CASE

Our patient was a telephone lineman, aged 30, who was admitted to the University Hospital on Feb. 2, 1929, with typical history, symptoms and signs of a basal lobar pneumonia of the left lung of three days' duration. During the next twelve days the signs and symptoms of the disease subsided, but on the following day there were a sharp rise in temperature, precordial pain and friction. Pericarditis was diagnosed. Pericardial fluid and a pulsus paradoxus followed, and 75 cc. of serosanguineous fluid containing *Streptococcus hemolyticus* and *S. viridans* was withdrawn by aspiration. Two days later extrapleural pericardiostomy was performed under local and regional anesthesia without infiltrating the pericardium or pleura. After portions of the fifth and sixth left costal cartilages were removed, the pericardium was incised longitudinally from the fourth intercostal space to the diaphragm, a distance of 6 cm. Two hundred and forty cubic centimeters of serofibrinous fluid was evacuated.

There were now exposed to view the lower anterior surfaces of the right and left ventricles, a portion of the inner surface of the pericardium, as well as a portion of the pericardial surface of the diaphragm (fig. 1). In addition, the entire surface of both ventricles, a part of the right auricle and all the pericardium overlying these portions of the heart, were within reach of certain of our examining instruments. The observations on the reactions to various sensory stimuli that are to be described, were then carried out. The condition of the patient

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* Throughout this article, the term "pericardium" will be used to denote the parietal pericardium and the term "heart" to denote myocardium and epicardium or visceral pericardium.

during these and subsequent observations was satisfactory, and he was not harmfully influenced by them. At the beginning of the operation his blood pressure was 112 systolic and 60 diastolic, his pulse rate 100 and his respirations 22. At the end of the operation they were, respectively, 118 and 60, 96 and 32. The pulse rate never rose above 108.

The operation was completed by sewing the incised edges of the pericardium to the pectoral fascia. This afforded excellent continuous drainage without the use of any tube or tissue. A surgical solution of chlorinated soda (Dakin's solution) and later 0.1 per cent solution of mercurochrome were introduced into the pericardial cavity six times daily, and drainage was aided by aspiration of the upper anterior and posterior recesses of the pericardial cavity with a catheter and syringe. Eleven days after operation all streptococci had disappeared, and six-

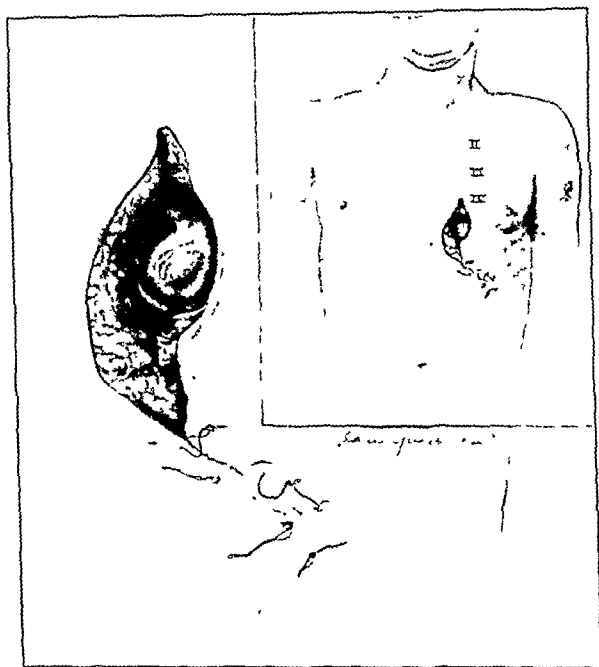


Fig. 1.—Drawings to scale of extrapleural pericardiostomy wound five days after operation. Part of the lower anterior surface of the right ventricle and a lesser part of the left ventricle are exposed. The diaphragm appears beneath the heart. The needle wound from the pericardial paracentesis may be seen in the left costophrenic angle.

teen days after operation no organisms could be found by smear, although diphtheroids and a few *Staphylococci aurci* were present by culture. In spite of this adequate control of infection in the pericardial cavity, the temperature and pulse did not improve correspondingly. This was attributed to residual infection in the lungs, of which there were signs.

As the pulse had become paradoxical, as the systolic blood pressure had dropped from 112 to 104 and as the pericardial cavity was surgically clean, we felt that the exposed heart should now be covered to combat further disabling thickening of the epicardium. This was done twenty-one days after first establishing drainage, by sliding a flap of skin and pectoral muscle over the opening, with the

patient under nitrous-oxide-oxygen anesthesia and in the Trendelenburg position. Just before operation the blood pressure was 104 systolic and 70 diastolic, the pulse rate was 108 and respirations 26. Twenty minutes later, toward the end of the operation, the systolic pressure was 92 and the diastolic 80, the pulse rate was 140 and respirations 48; thereafter the pulse rate and blood pressure could not be obtained. A state of paroxysmal auricular tachycardia with a rate of 192 at the heart persisted until death the following day. Also there were cyanosis and increasing dyspnea with signs of consolidation of both lungs.

At necropsy there were partly unresolved pneumonia of the left lower lobe and fresh consolidation of the remaining lobes of both lungs. Also there were a narrow empyema containing 140 cc. of pus, between the mediastinum and left lung, and a separate globular empyema of 200 cc. capacity in the costovertebral gutter directly back of the heart. The heart was not dilated and the pericardial cavity was clean, without any pocketing of pus (figs. 2 and 3). The thickness of the epicardium of the left ventricle twenty-three days after the onset of the pericarditis was as follows: base, anteriorly, 2 mm.; apex, anteriorly, from 3 to 6 mm.; base, posteriorly, 3 mm. or more, not including 2 mm. of fat; apex, posteriorly, 5 mm. or more, not including 1 mm. of fat. The thickness of the epicardium of the right ventricle was: base, anteriorly, 3 mm.; apex, anteriorly, from 3.5 to 4 mm.; base, posteriorly, 1.5 mm.; apex, posteriorly, 3.5 mm. The thickness of the epicardium of the right auricle, posteriorly, was 3 mm.

EXPERIMENTAL OBSERVATIONS

Reaction to Various Stimuli.—Investigations of the sensory reactions of the heart to various stimuli were carried out during the course of the pericardiostomy: during the frequent dressings; during several occasions when the heart was stimulated electrically to produce extrasystoles for electrocardiographic study; and during a period especially devoted to a systematic study of sensation sixteen days after operation, at which study Dr. Julian Moore aided us. During none of these experiments was the patient shocked or narcotized, except that prior to operation he had had 0.1 Gm. of morphine sulphate and the operation was conducted under local and regional anesthesia of the thoracic wall, but without direct infiltration of the pericardium. As the left side of the diaphragm was seen to be moving in the wound at each examination, it may be concluded that the motor and presumably the sensory paths of the left phrenic nerve were open.

The various points stimulated on the surface of the heart, and the inner surface of the pericardium, including the diaphragmatic pericardium, have been arbitrarily numbered for descriptive purposes in recording results (figs. 2 and 3). The location of the points that were exposed to view is exact. The position of those points that are between the heart and pericardium and out of sight has been carefully estimated and may be considered as accurate within fairly narrow limits. It is obvious that when an examining instrument was introduced far into the pericardial cavity, it was in contact with both heart and pericardium and that the produced sensation might have come from either. But when direct stimulation of the heart where it was not in contact with the pericardium did not produce the sensation produced by stimulation of heart and pericardium simultaneously, it may reasonably be concluded that this sensation came from the pericardium alone.

None of the stimuli used in these experiments apparently disturbed the rate, rhythm or force of the heart, except that electrical stimulation produced extrasystoles, and pressure of a catheter caused lessened excursion of the heart between systole and diastole, as noted subsequently. One of the two reflexes seen to be

produced by our manipulations was the "squirming" of the body and extremities when severe pain was caused by electrical stimulation of the heart and by certain stimuli of the pericardium; these movements may, of course, have been partly or wholly voluntary. The other reflex, the stimulation of coughing on irrigating the pericardial cavity, will be described in the section devoted to pressure sensation. No other reflexes were observed.

Pressure on the inner surface of the anterior pericardium caused reference of pain to the chest or abdomen. No other stimulus to the heart, pericardium or diaphragm caused reference of sensation to any part of the body. On several

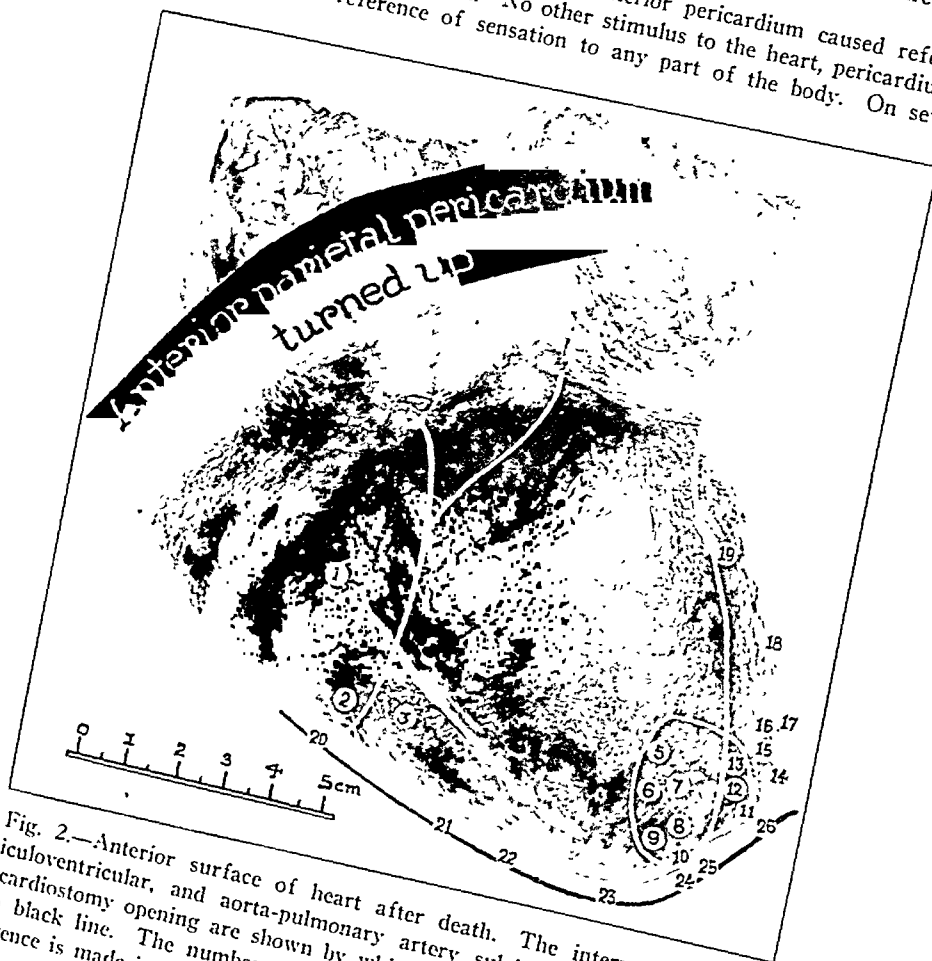


Fig. 2.—Anterior surface of heart after death. The interventricular, right auriculoventricular, and aorta-pulmonary artery sulci and the position of the pericardiostomy opening are shown by white ink. The diaphragm is represented by a black line. The numbers indicate points on the cardiac surface to which reference is made in the text.

occasions the patient was specifically asked about reference of sensation to the abdomen, back, shoulder, neck, arm and larynx.

Light touch with the tip of a finger or the end of a blunt-nosed hemostat to those portions of the ventricles and diaphragmatic pericardium (points 5, 6, 12, 13, 23, 24, 26)¹ exposed in the wound was not perceived as touch or any other

1. Throughout this article the numerically designated points refer to the position of correspondingly numbered points in figures 2 and 3.

sensation. Rubbing the ventricles (points 7, 10, 11, 12) rapidly for summation of stimuli, but not heavily, with the convex surface of a hemostat was felt as local pressure and not as pain.

Heavy pressure on the lower anterior and diaphragmatic surfaces of the ventricles (points 9, 12, 31, 33) with the convex surface of a curved hemostat (so heavy that the ventricular wall was partly invaginated, and with each systole the instrument was pushed away for a distance of about 1 cm.) was scarcely felt, and then only as local touch. It is possible that this sensation may have arisen in the posterior pericardium as a result of the heart being pushed against it.



Fig. 3.—Posterior surface of heart after death. The interventricular, right and left auriculoventricular sulci, and the position of the pericardiostomy opening are shown by white ink. The numbers indicate points on the cardiac surface to which reference is made in the text.

Pinching the lower anterior surface of the left ventricle (points 12, 14) with a 1 mm. deep bite of an Allis forceps caused no pain.

Pressure on the diaphragmatic pericardium (points 20, 21, 24, 26) was not identified as touch or pain but was described as "a feeling" or "sort of pressure." One point (point 24) beneath the right ventricle once had a sensation of slight pain.

Pressure forward against the inner surface of the pericardium at the right edge of the sternum in the fourth and fifth interspaces (points 1, 2) was felt as a sharp pain which radiated horizontally backward to the right midaxilla. The patient was able exactly to localize the position of the tip of the hemostat by

touching the overlying skin with the tip of his finger. Similarly induced pressure against the third left costal cartilage (point 19) was felt as pain which spread downward toward the left hypochondrium. Heavy pressure with the end of a hemostat against the posterior pericardium opposite both the right and the left ventricles (points 29, 30, 34) and against the left posterolateral pericardium (point 14) induced a sensation of pressure and not of pain. The right lateral wall of the pericardium could not be properly tested for heavy pressure because of a confusing sensation of pain from contact of the instrument with the right edge of the wound. Pinching the edges of the incised pericardium with a tissue forceps produced much pain.

When the finger was introduced into the pericardial cavity and swept around the ventricles to detect walled-off pockets of pus at the time of operation, severe local pain resulted. The observations of Capps and of Simenauer with regard to pressure on the pericardium will be cited under the section "Observations by Others." Their observations and ours are at variance; the different conditions under which their and our observations were made may account for the disagreement. Introduction of a catheter into the pericardial cavity toward the base of the heart both anteriorly (points 1, 19) and posteriorly (points 27, 34) caused moderately severe local pain. From ten days after operation, when the pericardium was thicker and presumably less sensitive, the pain was less severe and occasionally not present. As the pericardium shrank after drainage of its contained fluid, it became more difficult to introduce a catheter between the pericardium and the heart, and on several occasions when the catheter was left in place over the right ventricle for several minutes, the excursion of the ventricles between systole and diastole was seen to be lessened.

Several times when the pericardial cavity was being washed out by the installation of a surgical solution of chlorinated soda or a solution of mercurochrome through a catheter, the patient coughed up quantities of mucopurulent sputum—far more than at other times. He was not aware of any sensation, such as "tickling," as the stimulus to the urge to cough.

Pricking the lower anterior and diaphragmatic portions of the ventricles (points 5, 9, 12, 14, 16, 31, 32, 33) with the point of a needle to such a depth that a droplet of blood occasionally followed, was not felt in approximately half of the tests and in the others was felt only as touch, and the distinction between sharp and dull could not be made. Only at the apex of the heart (point 33) was every prick perceived as touch.

Many rapidly successive needle pricks of the diaphragm, about 1 cm. posterior to the level of the inner surfaces of the costal cartilages (points 22, 25) were only occasionally felt as local touch and never as pain.

At operation, piercing the cut edges of the incised pericardium caused sharp pain, and scratching its inner surface near to the incision with a needle caused slight pain.

The observations of Capps on piercing the pericardium and scratching its inner surface, and of Simenauer on pricking its outer surface, will be found under the section "Observations by Others."

At the time of operation the anterior surface of the left ventricle (points 12, 14) was grasped with two Allis forceps, 1 cm. apart, to the depth of about 1 mm., and the forceps were pulled away from one another with a force insufficient to tear the muscular fibers. This tension produced no local or referred anginal or anginoid pain.

Thermal sensation was tested by touching the heart, and the heart and pericardium simultaneously, with a thermometer that had been in hot and cold sterile

water At the moment of removing the instrument from the warm water it registered between 130 and 140 F. in all tests, and cooled slightly before it could be applied to the patient. On removing it from the cool water it registered between 40 and 50 F. and became slightly warmer before it could be applied. The cool thermometer placed against the granulating cut edge of the pectoral muscle was identified as cold, but the warm thermometer as neither hot nor cold. Tests for sensation of heat and cold were made on the exposed anterior surface of both ventricles (points 6, 12) and of the diaphragm (point 24) and simultaneously on the adjacent surfaces of pericardium and right and left ventricles (points 3, 4, 17, 18). In no instance could the patient distinguish either heat or cold. The only sensation produced was of touch or pain, the latter probably being due to pressure by the thermometer.

*Subjective Interpretation of Stimuli.**

Stimulus	Pericardium and Ventricles	Diaphragmatic Pericardium	Parietal Pericardium
Light touch . . .	0	0	—
Rubbing	Pressure	—	—
Heavy pressure	Touch	"A feeling" or pressure or slight pain	Posteriorly as pressure, anteriorly as pain, referred
Pinching	0	—	Severe pain
Finger or catheter in pericardial cavity	See parietal pericardium	—	Pain
Prickling	Occasionally as touch; constantly so at apex	Occasionally as touch	Sharp pain
Tension	0	—	—
Scratching	—	—	Slight pain
Heat . . .	0	0	0
Cold . . .	0	0	0
Vibration . . .	0	0	—
Electricity	Pain with extra-systoles	—	—
Two points of pressure	Differentiated only when one point on each ventricle	Not differentiated	—

* The ciphers indicate that no sensation was produced and the dashes indicate that sensibility was not tested

The temperature of the pericardial cavity was taken and is recorded, although unrelated to thermal sensation. An ordinary clinical thermometer was used and left in place five minutes or more. With the bulb of the thermometer near the right border of the sternum at about the fourth cartilage level (point 4), the temperature was 100.2 F. At the left border of the heart at the third interspace (point 18) and also beneath the right ventricle (point 28) the temperature was 100.7 F. At the time of this experiment the temperature by rectum was 101.3 F, by mouth 100.2 F. and by axilla 98 F.

Vibratory sensation was tested with tuning forks having 128 and 256 vibrations per second. These were placed directly on the anterior surfaces of both ventricles (points 5, 8, 12, 13) and on the diaphragmatic pericardium (points 24, 25). A sensation of vibration was nowhere perceived. When both the skin and the cut edge of the pectoral muscle were tested, the patient detected vibration when tuning fork 128 was used but not when fork 256 was employed, which produced only a sense of touch.

Electrical stimulation was effected by a Du Bois Raymond inductorium. With a key to deliver single make and break shocks we used a stimulating electrode

the points of which were about 3 mm. apart. The inductorium had 270 turns of wire on the primary coil and 5,000 turns on the secondary coil. We set the secondary coil to cover about three eighths of the primary coil. A single dry cell was used as a source of current.

Under these conditions the secondary coil delivered about 15 volts on the make shocks and 30 volts on the break shocks. It was found that such break shocks were approximately the ventricles' threshold for extrasystoles.

Such shocks were applied to points 3, 9, 14, 18 and 19 as well as to other points on the anterior surface of the right ventricle and to the base and apex of the left ventricle posteriorly; the exact position of these points will be fully given in our article devoted to consideration of the "Excitatory Process Observed in the Exposed Human Heart."²

Pain was produced on electrical stimulation when extrasystoles were produced. We cannot be certain, because of the difficulty of observing every extrasystole at the time the experiment was in progress, and before the electrocardiographic films were developed, that this was constantly so, nor that the pain did not sometimes occur when the heart was electrically stimulated without the production of extrasystoles.

At the time of operation, extrasystoles could not be produced by pricking, rubbing or pressing the heart.

In placing the blunt ends of two hemostats against the heart or diaphragmatic pericardium, care was taken that the parietal pericardium and thoracic wall were nowhere touched. Simultaneous pressure applied to points on the anterior surfaces of the right and left ventricles, 2 cm. apart (points 5, 13) and in another position at a distance of 2.5 cm. (points 10, 11) was repeatedly identified as two points of pressure. Pressure at two points on the right ventricle 2 cm. apart (points 7, 9) was identified as only one point. One point of pressure near the apex of the left ventricle (point 11) was repeatedly declared to be two points. Simultaneously applied pressure at two points 3 cm. apart on the diaphragmatic pericardium (points 24, 26) was not distinguished as two points. Single pressure elsewhere on the diaphragmatic pericardium (points 24, 26) was declared to be two points.

OBSERVATIONS BY OTHERS

Harvey³ wrote of one of his patients whose heart lay exposed, except for a "layer of fungous flesh as in old ulcers," as a result of an old defect in the overlying thoracic wall. Both Harvey and his friend "his Serene Majesty King Charles" felt the heart and found it without sense of touch, as the patient did not know when it was touched except by sight, or sensation through the external integument. Harvey concluded that the heart itself appears to be insensitive. This opinion has been widely quoted.

2. Barker, Paul S.; Macleod, A. Garrard; Alexander, John, and Wilson, Frank N.: *The Excitatory Process Observed in the Exposed Human Heart: I. The Spread of Excitation as Determined by Direct Leads; II. The Electrical Responses of Induced Premature Ventricular Contractions*, to be published in *Tr. A. Am. Phys.*, 1929, and elsewhere.

3. Harvey, William: *The Works of William Harvey, M.D.*, translated from the Latin by Robert Willis, M.D., London, printed for the Sydenham Society, 1847, pp. 382-384.

Luciani⁴ stated that "the afferent fibers from the heart are incapable of conveying clear or conscious sensations." Souligoux⁵ found that wounds of the heart are not in themselves painful and believed that the pain that occurs on the second or third day is due to inflammation of the pericardium or pleura. Lockwood⁶ stated that in a case of a missile in the heart, when the heart and pericardium were handled the patient did not complain of pain or distress, either cardiac or respiratory, although only local anesthesia was used. Auchincloss⁷ produced pain in the shoulder when he placed a clamp on the pericardium at its junction with the diaphragm. Cutler and Beck⁸ found that the pericardium is sensitive, especially when inflamed, and Cutler⁹ expressed the opinion that its upper and lateral portions are relatively much less sensitive than its lower portions.

Capps¹⁰ produced no pain when the pericardium and heart were touched, pressed or scratched with a silver wire introduced into the pericardial cavity through a cannula in four patients with pericardial effusion. In two patients he "tripped" the apex of the heart with the wire. One of these complained of a "queer aching sensation like pressure" in the stimulated area; the other had an uncomfortable feeling over the heart, and "skipped beats," but no pain. No pain occurred in two cases when the pericardium was pierced with the trocar and cannula at the level of the fourth intercostal space near the midclavicular line, but there was definite pain in the region of the left trapezius muscle in two other cases when the pericardium was pierced at the level of the fifth and sixth interspaces. In cases of dry pericarditis with friction rub and in cases of pericardial effusion, Capps' patients had local sensations of oppression, tightness and dyspnea, but never pain unless there was pleural involvement. He concluded that pericarditis is a painless disease and that mechanical irritation of the serous

4. Luciani, Luigi: *Human Physiology*, translated from the Italian by Frances A. Welby, edited by Dr. M. Cămis, London, MacMillan & Company, 1911, vol. 1, p. 335.

5. Souligoux, Charles: *Affections chirurgicales de la poitrine*, Paris, J. B. Baillière et fils, 1911, p. 106.

6. Lockwood, Ambrose L.: *Surgery of the Pericardium and Heart*, Arch. Surg. **18**:417 (Jan.) 1929.

7. Auchincloss, Hugh, in discussion on Peterson, Edward W.: *Suppurative Pericarditis*, Arch. Surg. **16**:377 (Jan.) 1928.

8. Cutler, Elliott C., and Beck, Claude: *Surgery of the Heart and Pericardium*, in Nelson's Loose-Leaf Living Surgery, New York, Thomas Nelson & Sons, 1927, vol. 4, chap. 4.

9. Cutler, Elliott C.: Verbal communication, March 27, 1929.

10. Capps, Joseph A.: *Pericardial Pain: An Experimental and Clinical Study*, Arch. Int. Med. **40**:715 (Nov.) 1927.

pericardium causes no pain. Lord¹¹ remarked on the infrequency of pain in pericarditis.

Simenauer¹² tested the sensation of the outer or pleural surface of the pericardium by approaching it with a thoracoscope-cautery outfit in three patients under treatment with artificial pneumothorax. Touch, light and heavy pressure, and pricking were not felt, but very heavy pressure at the level of the sixth rib was felt as an unpleasant sensation. In one case pressure on the pericardium in the region of the apex of the heart caused a pain like that in angina pectoris and a sensation of pressure on the mesial surface of the upper left arm and in a part of the lower arm.

SUMMARY

1. The response of the human heart, parietal and diaphragmatic pericardium to various forms of directly applied stimuli, has been determined in a patient whose heart was exposed by pericardiostomy for suppurative pericarditis.

2. The ventricles were insensitive to light touch. Rubbing was interpreted as pressure. Heavy pressure and pricking with a needle were interpreted as touch. Tension on the left ventricular wall caused no pain. Heat from 130 to 140 F. and cold from 40 to 50 F. were not identified. Application of tuning forks with 128 and 256 vibrations per second did not produce a sensation of vibration. Electrical stimulation caused pain only when extrasystoles occurred. Two blunt points of pressure simultaneously applied from 2 to 3 cm. apart on the right and left ventricles were identified as two points. Two points of pressure on the right ventricle were constantly said to be one point and one point of pressure on the left ventricle, two points.

3. The diaphragmatic pericardium did not feel light touch. Heavy pressure was interpreted as "a feeling" or pressure, and once as slight pain. Heat, cold and vibration were not identified. Two points of simultaneous pressure, 3 cm. apart, were not distinguished as two, and on two occasions one point of pressure was said to be two.

4. The parietal pericardium had a sensation of pressure when pressure was applied to the inner surface of its posterior and left posteriolateral walls. When pressure was applied forward against the anterior pericardium and thoracic wall, there was severe local and referred pain. Pain was also produced by sweeping the finger around the pericardial cavity, by pinching, pricking and scratching the inner surface of the pericardium. Heat and cold were not identified.

11. Lord, Frederick T., in discussion on Peterson, Edward W.: Suppurative Pericarditis, *Arch. Surg.* 16:375 (Jan.) 1928.

12. Simenauer, Erich: Die Sensibilität von Pleuren, Pericard und Peritonealüberzug des Diaphragma und besonderer Berücksichtigung des Nervus phrenicus, *Ztschr. f. Tuberk.* 48:273, 1927.

5. With the exception of pressure against the anterior pericardium, none of the stimuli applied to the heart or pericardium caused distant reference of sensation to any part of the body.

6. The stimuli used to evoke sensory response produced only two reflexes that we detected. One was the "squirming" of the body and the extremities on painfully stimulating the heart or pericardium. These movements may have been wholly or partly voluntary. The other reflex was the activation of coughing on irrigating the pericardial cavity.

7. Our observations do not justify conclusions as to the nerve paths concerned in the sensations produced.

ABSTRACT OF DISCUSSION

DR. E. A. GRAHAM, St. Louis: I want to congratulate Dr. Churchill particularly for the excellent result obtained in his case. I think it is interesting that Dr. Churchill, Dr. Allen and I should be thinking about the same thing at about the same time.

In the cases which I presented and talked about yesterday, I doubt whether the procedure of removing a portion of the pericardium would have had any particular value, although possibly in the case of the boy who died there might have been some beneficial effect from removing part of his pericardium.

In the two fatal cases which were shown yesterday, however, the hearts were greatly enlarged. I am anxious to know whether there is much scar tissue in the parietal pericardium with supposedly resultant constriction, and whether one can expect to find clinical or x-ray evidence of a greatly enlarged heart when the parietal pericardium is thick. I have not any literature bearing on that point. I am wondering if perhaps Dr. Churchill has. At any rate, it is a splendid result, and I congratulate Dr. Churchill most heartily.

I think the important point in Dr. Churchill's case, together with any possible importance in the remarks I made yesterday, is to emphasize the fact that there must be literally hundreds of cases of this sort in which the patients are going around not getting relief and having their condition regularly diagnosed as chronic heart disease. These conditions are amenable to surgical measures, the simple procedure of removing a section of the wall of the chest and, in some cases, a portion of the pericardium.

DR. HOWARD LILIENTHAL, New York: About five years ago I operated on a patient with a calcified pericardium, who had all the symptoms which Dr. Churchill has mentioned in his paper.

My only reason for speaking, other than to congratulate Dr. Churchill on his operation, is to say that in the case in which I performed an operation the pericardium had practically turned to stone. It was nearly a third of an inch in thickness. It felt and looked like an ordinary plaster cast. The patient had a huge liver with great ascites. She was a woman in the early twenties. My approach at that time was one which I think I would use again, and which I would strongly recommend. It is the first and only time I have used it, but I am sure it has great advantages in cases of this kind. I refer to the Duval-Barasty incision. It is a thoracolaparotomy, an incision longitudinally dividing the gladiolus and xiphoid. With the sternum shears, the surgeon incises sagittally

nearly to the umbilicus. With a rib spreader in the edges of a wound of that kind, a magnificent exposure is afforded. It does not seem to be at all shocking to the patient. In my own case it was practically bloodless. In these cases in which the disease is due, not to adhesion of the wall of the chest, but to the compression of the heart itself, it has the advantage of preserving the wall of the chest intact.

I failed to cure my patient, for I was unable to cut through that tremendously thick, tough cast that was over the heart without, what I considered, grave danger. I did go through it for about an inch and a half and entered what I conceived to be the auricle. There was some bleeding which yielded to packing. The patient was relieved and was walking about a few days afterward, although she had a little infection in the wound. She was discharged from the hospital somewhat improved. She lived a number of years afterward and then died of the disease.

DR. ALTON OCHSNER, New Orleans: There is just one point that I want to make with regard to the pathologic process and the technic.

I had the good fortune of serving as assistant to Schmieden in Frankfurt when he operated on three of these patients. The pathologic process is not only a fibrosis of the pericardium, but a marked fibrosis of the myocardium and epicardium. In two of these cases in which Schmieden performed an operation, it was impossible to tell when a part of the pericardium was removed. Frequently, the scalpel evidently went into the cardiac musculature.

I think Dr. Churchill is to be especially congratulated on the result he obtained. The results obtained in these cases are remarkable. They are all selected cases and, naturally, relatively few of them can be done; but I can agree with Dr. Churchill that in the selected cases the results are highly desirable and the operation should be done.

DR. ELLIOTT CARR CUTLER, Cleveland: I have had two experiences with similar cases, and would like to congratulate Dr. Churchill on his brilliant success.

The great difficulty for all of us is going to be to choose the right procedure even when we have such cases referred to us. The correct procedure may not be clear until the lesion is exposed.

This (indicating on a slide) is a case of calcified pericardium, with symptoms exactly similar to those described by Dr. Churchill. This is the heart after removal, and after removal of the pericardium. The calcification in this case extended all through the heart muscle. The diaphragm, the apex of the heart and the pericardium were one solid piece of bony substance. All the material that we could remove in the region of the right ventricle was removed. But a knife and scissors were ineffective and rongeurs were resorted to.

Cases in this group will vary between this sort with a calcified pericardium, in which there is a lime and salt deposit around the coronary vessels, and cases of simple, adherent mediastinitis.

In the simple case in which the pericardium is adherent to the wall of the chest, when the intrapericardial adhesions are not so bad, the surgeon may do a great deal of good. During the past year, I unfortunately did a simple rib resection—the ordinary Brauer operation—on a patient suspected of having this condition. The patient benefited little by it and died six or eight months later. Autopsy showed that the patient should have had a Delorme operation. On the other hand, in certain cases the Delorme operation, or any sort of operation, is dangerous and probably foolhardy. Diagnosis must be improved.

I think the lesson to learn from this case is that there are a great many cases of disease of the pericardium that the physicians will not diagnose unless pushed

by the surgeons. Physicians will let such patients sit in bed, giving them digitalis for ten years without any hope of benefit, and not let the surgeon, who may offer possible hope, even examine the case in consultation.

DR. POL. N. CORYLLOS, New York: I want to congratulate Dr. Churchill for his remarkable presentation and to express my deepest respect to the internist who in this case asked the collaboration of the surgeon. The case reported by Dr. Churchill shows the feasibility of Delorme's operation in well selected cases. Unfortunately, the selection of these cases is a great diagnostic problem because the clinical diagnosis of adhesive pericarditis is extremely difficult. Over a hundred years ago, Corvisart, and more recently, Norris and Landis have stressed this point. The latter concluded that pericarditis is to be suspected if in an endocarditis of rheumatic origin the cardiac failure is more marked than the endocardiac damage seems to warrant.

Another diagnostic problem is the determination of the variety of the adhesive pericarditis. The adhesions may be limited to the two layers of the pericardium alone, and might produce an incomplete or even complete obliteration of the pericardial cavity. Or they may extend to the surrounding structures, mediastinum, lungs and wall of the chest, as in the adhesive mediastinopericarditis of Pick. In the first variety the heart is encased in a thick solid, unextensible, sometimes calcified sac, which limits its movements as a tightly fitting glove limits the movements of the hand, according to the expression of Cutler. In that variety there may be no adhesions to the thoracic wall and consequently absence of the three clinical signs characteristic of the disease, namely, systolic retraction, diastolic shock and fixation of the apex notwithstanding changes of position of the patient. The heart may be extremely hypertrophied, but it also may be small because of the inextensibility of the thickened pericardium.

In all these cases an imperative indication is present. The pressure exerted on the heart, and the additional work imposed on it because of the tightness of the adhesions and the rigidity of the structures pulled on should be relieved. I shall go even further and say that in every case of rheumatic heart, especially when it is greatly hypertrophied, on which digitalis has no effect, surgical intervention is indicated, provided that the infectious process is arrested and the patient has still sufficient vitality to withstand operation. This will be the Brauer operation. In the presence of parietopericardiac adhesions the heart will be greatly relieved. In cases of simple "cor bovinum" even without pericardiac adhesions the decompression of the heart will often have a gratifying effect, as Dr. Graham has insisted on. This operation, harmless by itself, may serve as the first stage of the ulterior Delorme operation as suggested by Cutler.

I had the opportunity to perform the operation of Brauer three times with such gratifying results that I wonder why this operation is not performed more often.

I feel convinced that when internists will be more familiar with the indications and the benefits of this procedure, and less reluctant to consult the thoracic surgeon in cases of cardiac disease, a new and interesting era of medicosurgical treatment in cardiac diseases will begin, following the path of the evolution of the treatment of pulmonary diseases. Delorme, Beck, von Schmieden, Cutler and Churchill have already shown the way by their pioneer work.

DR. EDWARD D. CHURCHILL, Boston: My apology for bringing a single case report before this society is that in so many aspects it forms an ideal or textbook picture of this unusual condition and its treatment. There are two important reasons why this particular patient was what may be called an ideal case. First, the myocardium was sound; and second, the left ventricle was not involved in

the scar. In addition, I did not have to deal with an extensive degree of calcification such as Dr. Cutler and Dr. Lilienthal described.

Again, I was fortunate in finding a good line of cleavage so that the pericardium came off like the skin of an orange. In a few places adhesions required sharp dissection, but it was practically bloodless except in one spot on the surface of the heart which required a silk stitch ligature. Schmieden had a case in which the adherent pericardium blended with the myocardium with such intimacy that he had to hold his knife blade parallel to the surface and cut the thickened scar away in slices.

I agree with Dr. Graham that it is highly questionable as to whether the pericardium should be resected when one is doing a decompression for an enlarged heart. In such a case one is dealing with a weakened myocardium in addition to other factors.

In regard to the sternum-splitting incision used by Dr. Lilienthal, I believe that it is excellently adapted for exploration of the pericardial cavity and for the valvulotomy of Dr. Cutler. The advantage of the approach which I have pictured is that it leaves the patient with a Brauer cardiolysis in addition to the actual pericardial resection. As the heart becomes adherent after the lysis of adhesions, a flexible precordial area may well prevent further difficulty.

OPERATIONS ON THE INNOMINATE ARTERY

REPORT OF A SUCCESSFUL LIGATION

JAMES GREENOUGH, M.D.

COOPERSTOWN, N. Y.

In July, 1923, a white woman, aged 45, was seen in the outpatient department of Bellevue Hospital with a throbbing swelling in the right side of her neck. There were hard nodules about this area, and she was referred to the Memorial Hospital for treatment for metastatic carcinoma. A specimen removed from the neck showed chronic inflammatory disease. She returned to the clinic and was admitted to the First Surgical division on Nov. 6, 1923, for observation.

She was complaining of severe pain. On examination she appeared to be rather old for her age, with considerable arteriosclerosis. She had a tremor of the hands and head, which was diagnosed paralysis agitans. The aneurysm in the neck was thought to be of the right common carotid artery. The Wassermann reaction was negative. In view of her general condition operation did not seem advisable, and she was discharged on November 27.

She was readmitted to the hospital on Sept. 16, 1924, because of an increase in pain. It radiated down her right arm and to her chest. The pain and dyspnea kept her awake at night. Examination revealed practically the same condition as before. The heart was normal in size, but there was a diastolic murmur over the aortic area and a systolic murmur at the apex. There was a thrill over the aneurysm. The right and left radial pulses were equal. There was some question as to the site of the aneurysm at this time, opinion being divided between aneurysm of the carotid and aneurysm of the subclavian arteries. As the pain seemed to be much more severe operation was decided on, and on September 20, with the patient under general anesthesia, I explored the neck and ligated the innominate, carotid and subclavian arteries.

There was a diffuse fusiform aneurysm of the upper part of the innominate artery and the first portion of the subclavian artery. The carotid was enlarged just at its origin.

An incision 6 inches (15.2 cm.) long was made $\frac{1}{2}$ inch (1.3 cm.) above the right clavicle. This was deepened through platysma and fascia exposing the sternomastoid and clavicle. The sternomastoid was pulled laterally, and it was found that the aneurysmal mass was below the sternohyoid and sternothyroid and behind the clavicle. The clavicle was disarticulated from the sternum and turned laterally, exposing the retroclavicular tissues. The sternomastoid was cut at its insertion into the sternum, and the sternothyroid and sternohyoid were dissected away from the aneurysmal sac. The carotid, subclavian and innominate arteries were exposed in the bottom of the wound. It was found easy to surround the innominate artery without injuring the pleura. The carotid was distorted, being raised upward in the neck at its origin. The innominate artery was temporarily shut off and there was then felt no pulse in the right radial or right temporal arteries. However, at the end of five minutes there were still signs of circulation in the extremity, and it was deemed possible to ligate. Two ligatures of no. 2 chromic catgut, doubled, were passed around the innominate artery from within outward, and the innominate was ligated as close to the arch as could be reached without passing below the sternum. This was apparently proximal to the aneu-

rysmal dilatation. The carotid and subclavian arteries were ligated $\frac{1}{2}$ inch beyond their origins with double ligatures of no. 2 chromic catgut. The clavicle was sewed to the sternum with interrupted chromic catgut sutures through the capsule and periosteum. The muscles were approximated over the arteries with interrupted chromic catgut sutures. The skin was closed with silkworm gut, without drainage.

The right arm was wrapped in absorbent cotton immediately after operation. There was no pulse in the radial artery. The right side of the face was somewhat cold.

On the first day after operation, pulsation was felt in the radial and brachial arteries. The face had become warmer and was the same color on the right as on the left. The next day, the wound was dressed. The clavicle was displaced upward somewhat. The wound was clean. There was no pulsation in the aneurysm, but a definite pulsation in the right radial artery.

On the third day, the edges of the wound were slightly red. Pulsation in the radial artery seemed the same. There was slight pulsation at the site of operation, and the patient complained of some pain in the arm. The sutures were removed on the fifth day. There was considerable inflammation about the wound. A culture was taken which grew *Staphylococcus aureus*. On the seventh day, there was a distinct superficial infection about the wound, and it gaped slightly. The edges of the skin were cleaned with green soap, alcohol and ether and approximated with adhesive tape. The patient complained of headache. There seemed to be no difference in the circulation in the two arms. On the eighth day, the wound was becoming cleaner. There was no definite pulsation in the right carotid artery. The patient seemed much better. On the eleventh day, the wound was opened at the inner angle and a breakdown blood clot drained out. The temperature had risen to 104 F. the night before, although previous to this it had been about 100 F. On the twelfth day, the temperature was normal. The sinus, which had closed, was reopened, and there was a moderate amount of discharge. There was slight pulsation in the neck and in the region of the scar. The temperature on this day rose to 102 F. On the thirteenth day, a drain was inserted, and there was still considerable drainage.

For the next week there was a moderate amount of discharge. The temperature rose to between 101 and 102 F. each night, but the patient's general condition improved. She was allowed up on the twentieth day after operation. On the twenty-sixth day; it was noted that the clavicle seemed to be firmly adherent. The arm could be used. There was no evidence of paralysis, and the wound was rapidly healing. On the thirty-first day, a probe was passed into the sinus and apparently grated on the end of the clavicle, which seemed to be infected.

The patient was discharged thirty-three days after operation. No circulatory disturbances had been noted. At the time of discharge, the paralysis agitated had not changed. There was still a sinus which communicated with the inner end of the clavicle. There was pulsation in the right arm had dropped from 245 to 150.

The patient was readmitted to the hospital about one month later, on account of the discharge from the sinus, with a diagnosis of osteomyelitis of the inner end of the clavicle. On admission no radial pulse was felt, although the arm was normal in color and sensation. Motion of the arm was good. There was slight pulsation on the right side of the neck. There was a sinus at the medial end of the operative wound which extended down to the clavicle. Roentgen examination did not show the osteomyelitis.

On November 25, an incision was made over the right clavicle. The clavicle and sternum were separated by $\frac{1}{2}$ inch and the medial end of the clavicle had ebonized. The sinus was enlarged, the medial end of the clavicle was removed with a chisel and rongeur and an oval opening was left 1 inch (2.5 cm.) in diameter, with firm granulating tissue at the bottom. The wound was packed with dichloramine-T. The sinus was dressed daily, but the lower part did not heal as there was apparently still a portion of bare bone at the end of the clavicle. The patient was discharged on Jan. 1, 1925.

She was readmitted to the hospital on February 19 with an increase in the tenderness about the sinus, which had never closed. She had been at a convalescent hospital. No carotid pulse could be felt, nor was there any pulsation over the clavicle. The right radial pulse was fainter than the left. Blood pressure observations, on February 20, showed in the right arm a pressure of 120 systolic and 100 diastolic and in the left 174 systolic and 104 diastolic. On February 26, the sinus was opened again. The granulations were soft and unhealthy. Another portion of the clavicle, 1.5 by 0.5 cm., had sequestered and was removed. A portion of the bone over the sequestrum was removed, and an oval opening packed with iodoform gauze was left. Granulations gradually filled in and the patient was discharged to the City Hospital on April 6, with a small sinus. She was discharged from that hospital on April 17, 1925, and lost from observation. At that time there was a sinus still communicating with the inner end of the clavicle. The aneurysm was apparently healed as there was no mass and no pulsation. The pulse in the right radial artery was less than in the left and was absent in the right carotid. The use of the arm was interfered with by the osteomyelitis of the clavicle which had not healed.¹

DATA FROM THE LITERATURE

Including my case, I have been able to find in the literature reports of 91 cases of operation on the innominate artery (table 1). They may be grouped as follows:

The innominate artery alone was ligated in 43 cases (table 2). These operations were performed for subclavian aneurysm in 26 cases, carotid aneurysm in 4, bifurcation aneurysm in 4, multiple aneurysm in 4, wounds in 4, and 1 case in which the diagnosis was unknown. There were 28 deaths and 15 recoveries, a mortality of 65 per cent. There were previous or subsequent ligations in 13 of the cases, or about 30 per cent. Of the 37 aneurysms, 10 are reported cured, 9 clotted and 3 improved. The aneurysm was thus definitely benefited in 59 per cent.

The innominate and carotid arteries were ligated in 20 cases (table 3). The operation was performed for subclavian aneurysm in 13 cases, bifurcation aneurysm in 2, multiple aneurysm in 2, innominate aneurysm in 1, stab wound in 1 and in 1 case in which the diagnosis was unknown. There were 9 deaths and 11 recoveries, a mortality of 45 per cent. There were previous or subsequent ligations in 6 of the cases, or 30 per cent. Of the 18 aneurysms, 6 were reported cured, 2 clotted and 4 improved. Thus 66 per cent of the aneurysms were benefited.

1. J. A. McCreery, Chief of the First Surgical Division, Bellevue Hospital, gave me permission to report this case.

TABLE 1.—Data on Ninety-One Cases of Operation on the Innominate Artery

Case	Surgeon	Date	Diagnosis	Operation	Result
1	V. Mott.....	1818	Subclavian aneurysm	Innominate ligation	Death
2	Graefe.....	1822	Subclavian aneurysm	Innominate ligation	Death
3	Norman.....	1824	Subclavian aneurysm	Innominate ligation	Death
4	Arendt.....	1827	Subclavian aneurysm	Innominate ligation	Death
5	Hall.....	1830	Subclavian aneurysm	Ligature through innominate	Death
6	W. H. Porter.....	1831	Subclavian aneurysm	Attempted innominate ligation	Recovery
7	Bland.....	1832	Subclavian aneurysm	Innominate ligation	Death
8	Bujalsky.....	1833	Subclavian aneurysm	Innominate ligation	Death
9	Unknown, reported by Dupuytren	1834	Unknown	Innominate ligation	Death
10	Kuhl.....	1836	Neoplasm of face	Subclavian and carotid ligation thought to be innominate	Death
11	Lizar.....	1837	Subclavian aneurysm	Innominate ligation	Death
12	Hoffman.....	1839	Subclavian aneurysm (2)	Attempted innominate ligation	Death
13	Hutin.....	1841	Axillary wound	Innominate ligation	Death
14	Key.....	1844	Innominate and subclavian aneurysm	Attempted innominate ligation	Death
15	Peixoto.....	1851	Tumor of ear	Precautionary innominate ligature, not tied	Recovery
16	Pirogoff.....	1852	Subclavian aneurysm	Innominate ligation	Death
17	Gore.....	1856	Subclavian aneurysm	Innominate ligation	Death
18	Cooper.....	1859	Subclavian and carotid aneurysm	Innominate ligation	Death
19	Cooper.....	1860	Subclavian aneurysm	Innominate ligation	Death
20	Smyth.....	1864	Subclavian aneurysm	Innominate and carotid ligation	Recovery
21	Lynch.....	1867	Wound	Innominate ligation	Death
22	G. H. Porter.....	1867	Subclavian aneurysm	Innominate acupressure 60 hours	Death
23	Bickersteth.....	1868	Subclavian aneurysm	Innominate ligation	Death
24	A. B. Mott.....	1868	Unknown	Innominate and carotid ligation	Death
25	Partridge.....	1870	Carotid aneurysm	Innominate ligation	Death
26	O'Grady.....	1873	Axillary and subclavian aneurysm	Innominate and carotid ligation	Death
27	Buchanan.....	1880	Subclavian aneurysm	Innominate ligation	Death
28	Thomson.....	1882	Subclavian aneurysm	Innominate ligation	Death
29	Banks.....	1883	Subclavian aneurysm	Innominate and carotid ligation	Death
30	Bull.....	1884	Subclavian aneurysm	Innominate, carotid and vertebral ligation	Death
31	Annandale.....	1885	Subclavian aneurysm	Pressure on innominate artery	Death
32	Heiferich.....	1886	Subclavian aneurysm	Innominate, carotid and subclavian ligation	Death
33	May.....	1886	Subclavian aneurysm	Innominate ligation	Death
34	Durante.....	1887	Subclavian aneurysm	Innominate, carotid and subclavian ligation	Death
35	Lewtas.....	1889	Wound		Recovery
36	Twynam.....	1889	Subclavian aneurysm		Death
37	Jacobson.....	1890	Subclavian aneurysm	Innominate and carotid ligation	Death
38	Heiferich.....	1890	Bifurcation aneurysm	Attempted innominate ligation	Death
39	Copplager.....	1893	Subclavian aneurysm	Innominate and carotid ligation	Recovery
40	Hernandez.....	1894	Wound	Innominate ligation, carotid clamped	Recovery
41	Parham.....	1894	Bifurcation aneurysm	Attempted innominate ligation	Death
42	Symonds.....	1894	Subclavian aneurysm	Innominate and carotid ligation	Recovery
43	Burrell.....	1895	Subclavian aneurysm	Innominate ligation	Death
44	Harte.....	1896	Wound	Innominate, carotid, subclavian, jugular vein ligation	Death
45	Gay.....	1896		Innominate ligation	Death
46	Schumpert.....	1898		Innominate ligation	Death
47	Moynihan.....	1898		Innominate and carotid ligation	Death
48	Bennett.....	1898		Innominate ligation	Death
49	Curtis.....	1899		Innominate ligation	Recovery
50	DeLaup.....	1900		Innominate ligation	Death
51	von Ruediger.....	1901	clavian aneurysm Subclavian aneurysm	Innominate and subclavian ligation; sac partially excised	Death
52	Ballance.....	1902	Bifurcation aneurysm	Innominate and carotid ligation	Death

TABLE 1—Data on Ninety-One Cases of Operation on the Innominate Artery—Continued

Case	Surgeon	Date	Diagnosis	Operation	Result
53	Persons	1901	Hemorrhage	Innominate ligation	Death
54	Sheen	1901	Subclavian aneurysm	Innominate and carotid ligation	Recovery
55	Salgo	1901	Traumatic carotid aneurysm	Innominate ligation	Recovery
56	Salgo	1905	Traumatic varicose subclavian aneurysm	Innominate ligation	Recovery
57	Halsted	1905	Subclavian aneurysm	Partial innominate ligation	Recovery
58	Cunco	1905	Innominate and aortic aneurysm	Innominate ligation	Recovery
59	Curtis	1907	Subclavian aneurysm	Innominate ligation	Death
60	Halsted	1907	Bifurcation aneurysm	Innominate ligation	Recovery
61	Burns	1907	Subclavian aneurysm	Innominate ligation	Recovery
62	Myles	1908	Subclavian aneurysm	Innominate and carotid ligation, carotid cut	Death
63	Hirzen	1908	Traumatic subclavian aneurysm	Innominate, carotid and subclavian arteries, subclavian and jugular vein ligated, carotid cut	Recovery
64	Kimura	1908	Bifurcation aneurysm	Innominate, carotid and subclavian ligation, all cut and sac excised	Recovery
65	Ballance	1909	Bifurcation aneurysm	Innominate ligation	Death
66	Sargent	1909	Innominate aneurysm	Innominate and carotid ligation	Recovery
67	Morf	1911	Subclavian aneurysm	Innominate and carotid ligation	Recovery
68	Ballance	1911	Subclavian aneurysm	Innominate ligation	Recovery
69	Morison	1912	Subclavian aneurysm	Innominate and carotid ligation	Recovery
70	Halsted	1912	Recurrent subclavian aneurysm	Innominate ligation	Recovery
71	Hamann	1913	Subclavian aneurysm	Innominate and carotid ligation	Recovery
72	Thompson	1914	Subclavian aneurysm	Innominate ligation	Death
73	Lessnol	1915	Innominate and carotid aneurysm	Innominate ligation	Recovery
74	Hamann	1915	Subclavian aneurysm	Innominate and carotid ligation	Recovery
75	Hamann	1916	Bifurcation aneurysm	Innominate and carotid ligation	Death
76	Coughlin	1916	Subclavian aneurysm	Innominate and carotid ligation	Recovery
77	Sinclair	1916	Traumatic carotid aneurysm	Innominate ligation	Recovery
78	Coughlin	1916	Unknown	Attempt to ligate innominate	Death
79	Makins	War	Gun shot wound subclavian	Innominate clamped temporarily, subclavian ligation	Death
80	Makins	War	Traumatic subclavian varicose aneurysm	Innominate, subclavian artery and subclavian vein ligation, sac excised	Recovery
81	Sauerbruch	War	Gun shot wound, innominate	Suture of innominate	Death
82	Halsted	1918	Carotid aneurysm	Innominate ligation	Recovery
83	Reid	1918	Innominate aneurysm	Attempt to ligate innominate	Death
84	Halsted	1918	Gun shot wound, innominate	Suture of innominate	Recovery
85	Ballance	1918	Subclavian aneurysm	Innominate ligation	Recovery
86	Juckelson	1919	Carotid aneurysm	Innominate, carotid, subclavian ligation, sac partly excised	Recovery
87	Hertzler	1922	Traumatic subclavian aneurysm	Innominate ligation	Recovery
88	Holman	1922	Traumatic, subclavian aneurysm, varicose	Innominate, subclavian artery and vein and sac sutured	Recovery
89	Greenough	1924	Bifurcation aneurysm	Innominate, carotid and subclavian ligation	Recovery
90	Sauerbruch	1925	Tumor thyroid rupture of innominate	Innominate suture	Recovery
91	Ellis	1927	Traumatic bifurcation aneurysm	Innominate ligation and subclavian suture, sac packed	Recovery

TABLE 2—*Innominate Ligations*

No	Diagnosis	Result	Date	Other Ligations	Aneurysm
1	Subclavian aneurysm	Death	25th day		Infected
2	Subclavian aneurysm	Death	67th day		
3	Subclavian aneurysm	Death	5th day		
4	Subclavian aneurysm	Death	8th day		
7	Subclavian aneurysm	Death	18th day		Temporary improvement
8	Subclavian aneurysm	Death	5th day		
9	Unknown	Death			Clotted
11	Subclavian aneurysm	Death	21st day	Subclavian	
12	Wound	Death	12th hour		
16	Subclavian aneurysm	Death	2d day		Improved
17	Subclavian aneurysm	Death	16th day		
18	Carotid and subclavian aneurysm	Death	9th day		Clotted
19	Subclavian aneurysm	Death	41st day		Clotted
21	Wound	Death	12th day	Carotid Innominate pressure Carotid	Clotted
23	Subclavian aneurysm	Death	6th day		
25	Carotid aneurysm	Death	1½ hours		Clotted
27	Subclavian aneurysm	Death			
28	Subclavian aneurysm	Death	40th day		Partly clotted
33	Subclavian aneurysm	Death	18th day		
35	Wound	Recovery	43d day		Clotted
43	Subclavian aneurysm	Death	104th day	Carotid	
45	Subclavian aneurysm	Death	41st day		
46	Bifurcation aneurysm	Death	9th day		
48	Bifurcation aneurysm	Death	3d day		
49	Subclavian aneurysm	Recovery	11 months	Carotid and subclavian	Cured
50	Subclavian and bifurcation aneurysm	Death	18th day	Carotid and vertebral	Clotted
53	Wound	Death			Cured
55	Traumatic carotid aneurysm	Recovery	9 months	Carotid	
56	Traumatic varicose subclavian aneurysm	Recovery	7 months	Subclavian artery and vein; excision of sac	Cured
57	Traumatic varicose subclavian aneurysm	Recovery	15 years		Cured
58	Aortic and innominate aneurysm	Recovery	5 years		Improved
59	Subclavian aneurysm	Death	4th day	Carotid	Clotted
60	Bifurcation aneurysm	Recovery			Cured
61	Subclavian aneurysm	Recovery	11 months		Cured
65	Bifurcation aneurysm	Death	21st day		
68	Subclavian aneurysm	Death	30 hours		Improved
70	Subclavian aneurysm	Recovery	1 month	Subclavian	
72	Subclavian aneurysm	Recovery	47th day		Clotted
73	Innominate and carotid aneurysm	Death	67th day		
		Recovery			Cured
77	Traumatic carotid	Recovery	3 months		Cured
82	Carotid aneurysm	Recovery	6 years	Carotid	Cured
85	Subclavian aneurysm	Recovery			Cured
87	Subclavian aneurysm	Death	2 years	Carotid and vertebral	Unchanged
		Recovery	7 months		

TABLE 3—*Innominate and Carotid Ligations*

No	Diagnosis	Result	Date	Other Ligations	Aneurysm
20	Subclavian aneurysm	Recovery		Vertebral	Improved; recurred
21	Unknown	Death	17 months		
26	Subclavian and axillary aneurysm	Death	22d day		Ruptured
		Death	15 hours		
29	Subclavian aneurysm	Death	104th day	Subclavian	Improved
36	Subclavian aneurysm	Death	18 hours		
37	Subclavian aneurysm	Death	10th day		Clotted
39	Subclavian aneurysm	Recovery	2½ years		Clotted
40	Wound	Recovery	6 years		Cured
42	Subclavian aneurysm	Recovery	5 years		Cured
		Death			
47	Subclavian (2) and axillary aneurysm	Death	1 hour	Subclavian and axillary	Second ruptured
		Death			
52	Bifurcation aneurysm	Death	1½ days		Cured
54	Subclavian aneurysm	Recovery	9 months	Subclavian	
62	Subclavian aneurysm	Death	1 month	Carotid	Cured
66	Innominate aneurysm	Recovery			
		Death	17 months		Cured
67	Subclavian aneurysm	Recovery	6 years		
69	Subclavian aneurysm	Recovery	2 years		Improved
71	Subclavian aneurysm	Recovery	13 months		
74	Subclavian aneurysm	Recovery	2 months		Cured
75	Bifurcation aneurysm	Death	4 days	Partial innominate	Improved
76	Subclavian aneurysm	Recovery	2 years		Cured

The innominate, carotid and subclavian arteries were ligated with or without associated veins in 6 cases (table 4). This was done for subclavian aneurysm twice, bifurcation aneurysm twice, carotid aneurysm once and gunshot wound once. Four patients recovered and 2 died, a mortality of 33 per cent. There was previous ligation in 1, or 16.66 per cent, of the cases. Of the 5 aneurysms, 4 were cured, or 80 per cent.

The innominate and subclavian arteries were ligated in 4 cases with or without associated veins (table 5). Three ligations were performed for subclavian aneurysm and 1 for bifurcation aneurysm. There was

TABLE 4—*Innominate, Carotid and Subclavian Ligations*

No	Diagnosis	Result	Date	Other Ligations	Aneurysm
32	Subclavian aneurysm	Death	2d day		
44	Wound	Death	Hour	Carotid	
63	Subclavian aneurysm	Recovery	4 months		Cured
64	Bifurcation aneurysm	Recovery	...		Cured
86	Carotid aneurysm	Recovery	6 years		Cured
89	Bifurcation aneurysm	Recovery	19 months		Cured

TABLE 5—*Innominate and Subclavian Ligations*

No.	Diagnosis	Result	Date	Other Ligations	Aneurysm
51	Subclavian aneurysm	Death	Hour		
80	Traumatic varicose subclavian aneurysm	Recovery	12th day		Cured
88	Traumatic varicose subclavian aneurysm	Recovery	1 year		Cured
91	Bifurcation aneurysm	Recovery	6 months		Cured

TABLE 6—*Innominate, Carotid and Vertebral Ligations*

No	Diagnosis	Result	Date	Other Ligations	Aneurysm
30	Subclavian aneurysm	Death	33d day		Infected
34	Subclavian aneurysm	Death	16th day		

1 death, a mortality of 25 per cent. There were no previous or subsequent ligations, and the aneurysm was cured in 3 cases, or 75 per cent.

The innominate, carotid and vertebral arteries were ligated for subclavian aneurysm in 2 cases (table 6). Both patients died with no benefit to the aneurysm, a mortality of 100 per cent. There were no previous or subsequent ligations.

Figure 1 shows a comparison of the mortality, the benefit to the aneurysm and the associated operations in these various groups.

Unsuccessful attempts to ligate the innominate artery were made 9 times. Temporary pressure was applied 4 times. The vessel was sutured 3 times.

The causes for operation were aneurysm, 75; injury, 9; hemorrhage from remote pathologic process, 3, and in 4 the cause was not given.

The 75 aneurysms were grouped as follows: subclavian, 50; bifurcation, 9; carotid, 6; innominate, 2; multiple, 8; involving the subclavian, 6 times; innominate, 3; carotid and axillary, 2 each; bifurcation and aorta, 1 each.

The total mortality for the series is 59.3 per cent. For purposes of discussion, I have divided the series into three groups. Table 7 shows the cases that occurred previous to 1880, or in the preaseptic period. There were 27 cases with 3 recoveries, a mortality of 89 per cent. Table 8 shows the cases that occurred from 1880 to an arbitrary point in 1904, when the mortality rate suddenly began to drop. There

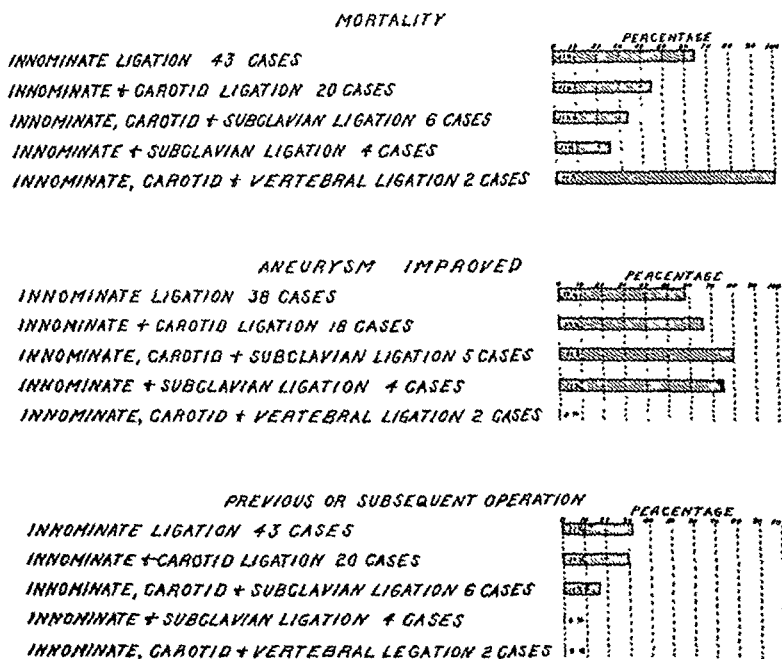


Fig. 1.—Graphs showing mortality, improvement and additional operations in ligations of the innominate artery and its branches.

were 26 cases with 5 recoveries, a mortality of 81 per cent. Table 9 shows the 38 cases that occurred from 1904 to date in which there were 29 recoveries, a mortality of 24 per cent. Figure 2 shows the mortality by tens from the beginning. This also demonstrates the sharp drop in the mortality rate about 1904.

Examination of the causes of death may show the reason for this change. Table 10 gives the causes of the 54 deaths as follows: sup-
puration, suppuration and hemorrhage, or hemorrhage, 30, or 56 per cent; shock, 11, and cerebral lesions, 7. Thus 48, or 89 per cent, are definitely due to causes arising from the operation itself. Infection is

the primary cause for hemorrhage. Fifty-six per cent of the deaths can be traced to infection then. If this is the case, there must be some factors in addition to asepsis which account for the drop in the mortality rate because it does not occur in 1880 with the introduction of asepsis but almost twenty-five years later, in 1904.

I believe that the improvement is due to greater facility in operating, as shown by the development of the operative exposure, the improvement in ligature material and application of the ligature, and to closure of the wound without drainage.

The incision advocated by Mott, who performed the first ligation in 1818, was a V type with one limb along the border of the sternomastoid

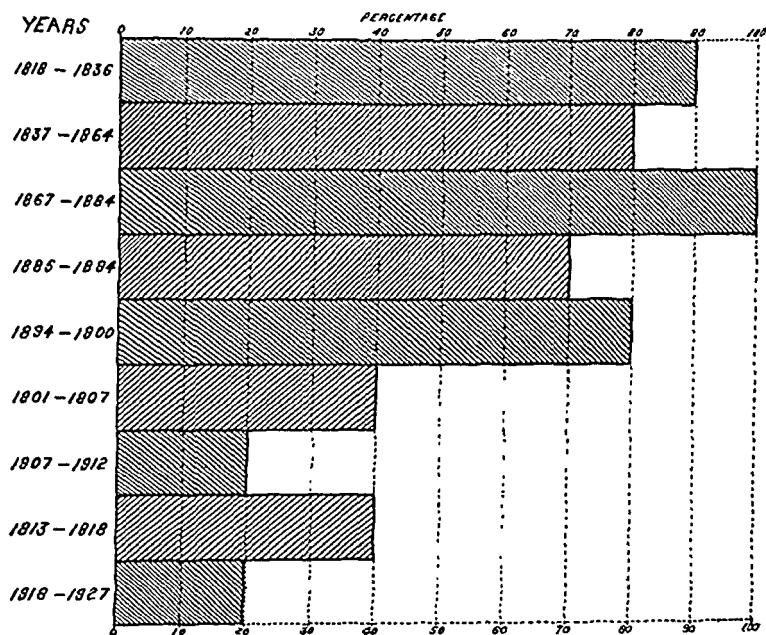


Fig. 2.—Mortality in operations on the innominate artery in groups of ten.

muscle, the other above the clavicle. This has been described with slight modification in 27 cases. A single incision in the midline along the sternomastoid or along the clavicle has been used 28 times. Various other types of right angle incisions making flaps to be drawn back in various ways have been used occasionally (fig. 3).

Of more interest, however, is the gradual development of bone resection in addition to the soft part dissection (fig. 4). In 1859, Cooper, who performed the eighteenth ligation of the series, first removed part of the bony thoracic wall. He resected parts of the manubrium and the right clavicle. This gave a better exposure and made the operation simpler.

In the 27 cases that occurred before 1880, when the mortality was 89 per cent, there were 3 bone resections. In the 26 cases that occurred from 1880 to 1904, when the mortality was 81 per cent, there were 11

TABLE 7—Cases from 1818 to 1880

No	Surgeon	Date	Ligation	Result
1	V Mott	1818	Innominate	Death
2	Graefe	1822	Innominate	Death
3	Norman	1824	Innominate	Death
4	Arendt	1827	Innominate	Death
5	Hall	1830	Needle through innominate	Death
6	W H Porter	1831	Attempted innominate	Recovery
7	Bland	1832	Innominate	Death
8	Bujalsky	1833	Innominate	Death
9	Unknown	1834	Innominate	Death
10	Kuhl	1836	Attempted innominate	Death
11	Lizar	1837	Innominate	Death
12	Hoffman	1839	Attempted innominate	Death
13	Hutin	1841	Innominate	Death
14	Key	1844	Attempted innominate	Death
15	Peixoto	1851	Precautionary innominate	Recovery
16	Pirogoff	1852	Innominate	Death
17	Gore	1856	Innominate	Death
18	Cooper	1859	Innominate	Death
19	Cooper	1860	Innominate	Death
20	Smyth	1864	Innominate and carotid	Recovery
21	Lynch	1867	Innominate	Death
22	G H Porter	1867	Pressure on innominate	Death
23	Bickersteth	1868	Innominate	Death
24	A B Mott	1868	Innominate and carotid	Death
25	Partridge	1870	Innominate	Death
26	O'Grady	1873	Innominate and carotid	Death
27	Buchanan	1880	Innominate	Death

Cases, 27; deaths, 24, mortality, 89 per cent

TABLE 8—Cases from 1882 to 1904

No	Surgeon	Date	Ligation	Result
28	Thomson	1882	Innominate	Death
29	Banks	1883	Innominate and carotid	Death
30	Bull	1884	Innominate	Death
31	Annandale	1884	Pressure on	Death
32	Helfferich	1886	Innominate	Death
33	May	1886	Innominate	Death
34	Durante	1887	Innominate, carotid and vertebral	Death
35	Lewtas	1889	Innominate	Recovery
36	Twynham	1889	Innominate and carotid	Death
37	Jacobson	1890	Innominate and carotid	Death
38	Helfferich	1890	Attempted innominate	Death
39	Copplinger	1893	Innominate and carotid	Recovery
40	Hernandez	1894	Innominate and carotid	Recovery
41	Parham	1894	Attempted innominate	Death
42	Symonds	1894	Innominate and carotid	Recovery
43	Burrell	1895	Innominate	Death
44	Harte	1896	Innominate, carotid, subclavian and jugular vein	Death
45	Gay	1896	Innominate	Death
46	Schumpert	1896	Innominate	Death
47	Moynihan	1898	Innominate and carotid	Death
48	Bennett	1898	Innominate	Death
49	Curtis	1899	Innominate	Recovery
50	DeLaup	1900	Innominate	Death
51	von Ruediger	1901	Innominate and subclavian	Death
52	Ballance	1902	Innominate and carotid	Death
53	Pearson	1904	Innominate	Death

Cases, 26, deaths, 21; mortality, 81 per cent

bone resections. In the 38 cases that occurred since 1904, when the mortality was 24 per cent, there were 23 bone resections. In the 37 cases in which bone resection was done there were 17 deaths, or a mortality of 46 per cent. In the 54 cases in which bone resection was

not performed or is not mentioned, there were 37 deaths, or a mortality of 68.5 per cent.

Except when the bifurcation is high, the work on the vessels has to be done by palpation when the thoracic bony wall is not resected. As evidence of this I have found in the cases in which ligations were attempted, without bone resection, 2 cases in which the innominate could not be dissected out, 1 in which the carotid and the subclavian were tied together by mistake for the innominate, 1 in which the

TABLE 9.—Cases from 1904 to 1927

No.	Surgeon	Date	Ligation	Result
54	Sheen.....	1904	Innominate and carotid.....	Recovery
55	Salgo.....	1904	Innominate	Recovery
56	Salgo.....	1905	Innominate and cut.....	Recovery
57	Halsted.....	1905	Partial innominate	Recovery
58	Cunco.....	1905	Innominate	Recovery
59	Curtis.....	1907	Innominate	Death
60	Halsted.....	1907	Innominate	Recovery
61	Burns.....	1907	Innominate	Recovery
62	Myles.....	1908	Innominate and carotid.....	Death
63	Herzen.....	1908	Innominate, carotid, subclavian and subclavian vein	Recovery
64	Kimura.....	1908	Innominate, carotid and subclavian.....	Recovery
65	Ballance.....	1909	Innominate	Death
66	Sargent.....	1909	Innominate and carotid.....	Recovery
67	Morf.....	1911	Innominate and carotid.....	Recovery
68	Ballance.....	1911	Innominate	Recovery
69	Morison.....	1912	Innominate and carotid.....	Recovery
70	Halsted.....	1912	Innominate	Recovery
71	Hamann.....	1913	Innominate and carotid.....	Recovery
72	Thompson.....	1914	Innominate	Death
73	Lessnol.....	1915	Innominate	Recovery
74	Hamann.....	1915	Innominate and carotid.....	Recovery
75	Hamann.....	1916	Innominate and carotid.....	Death
76	Coughlin.....	1916	Innominate and carotid.....	Recovery
77	Sinclair.....	1916	Innominate	Recovery
78	Coughlin.....	1916	Attempted innominate	Death
79	Makins.....	War	Innominate clamped, subclavian ligated.....	Death
80	Makins.....	War	Innominate, subclavian and subclavian vein....	Recovery
81	Sauerbruch.....	War	Innominate suture	Death
82	Halsted.....	1918	Innominate	Recovery
83	Reid.....	1918	Attempted innominate	Death
84	Halsted.....	1918	Innominate suture	Recovery
85	Ballance.....	1918	Innominate	Recovery
86	Juckelson.....	1919	Innominate, carotid and subclavian.....	Recovery
87	Hertler.....	1922	Innominate	Recovery
88	Holman.....	1922	Innominate, subclavian and subclavian vein....	Recovery
89	Greenough.....	1924	Innominate, carotid and subclavian.....	Recovery
90	Sauerbruch.....	1925	Innominate suture	Recovery
91	Flint.....	1927	Innominate and subclavian.....	Recovery

Cases, 38; deaths, 9; mortality, 24 per cent

aneurysm needle was passed through the innominate artery, and 1 in which the patient died from the shock of pulling on the aorta.

When the clavicle and sternum, with or without the first rib, are partially resected, the patients show practically no disability. Fibrous union develops which is sufficient for the function of the arm. The operation of ligation, whether for aneurysm or vascular injury, is undertaken as a life-saving measure. The advantages of exposure certainly outweigh the disadvantages of slight disability due to bone resection.

In my own case I dislocated the sternal end of the clavicle. The infection and nonunion following this procedure detracted from the

TABLE 10.—Deaths Occurring Following Ligations

No.	Diagnosis	First Ligation	Second Ligation	Date	Cause of Death
1	Subclavian aneurysm	Innominate	25th day	Suppuration and hemorrhage
2	Subclavian aneurysm	Innominate	67th day	Suppuration and hemorrhage
3	Subclavian aneurysm	Innominate	5th day	Pericarditis
4	Subclavian aneurysm	Innominate	8th day	Suppuration, pneumonia, cerebral lesion
5	Subclavian aneurysm	Attempted innominate	5th day	Suppuration and pericarditis
7	Subclavian aneurysm	Innominate	18th day	Suppuration and hemorrhage
8	Subclavian aneurysm	Innominate	5th day	Suppuration, pericarditis, empyema
9	Subclavian aneurysm	Innominate	Hemorrhage
10	Neoplasm.....	Attempted innominate	3d day
11	Subclavian aneurysm	Innominate	21st day	Internal and external hemorrhage
12	Subclavian aneurysm	Attempted innominate	85th day	Exhaustion
13	Wound.....	Subclavian	Innominate	12 hours	Shock
14	Innominate, subclavian aneurysm	Attempted innominate	25th day	Pressure on trachea
16	Subclavian aneurysm	Innominate	2d day	Suppuration, pneumonia, meningitis
17	Subclavian aneurysm	Innominate	16th day	Suppuration and hemorrhage
18	Subclavian and carotid aneurysm	Innominate	9th day	Suppuration and nephritis
19	Subclavian aneurysm	Innominate	41st day	Suppuration and hemorrhage
21	Wound.....	Carotid	Innominate	12th day	Hemorrhage
22	Subclavian aneurysm	Innominate pressure	10th day	Hemorrhage
23	Subclavian aneurysm	Innominate pressure	Innominate	6th day	Hemorrhage
24	Innominate and carotid	23d day	Aneurysm ruptured, hemorrhage
25	Carotid aneurysm....	Carotid	Innominate	1½ hours	Shock
26	Subclavian aneurysm	Innominate and carotid	15 hours	Cerebral effusion
27	Subclavian aneurysm	Innominate	Shock
28	Subclavian aneurysm	Innominate	40th day	Suppuration and hemorrhage
29	Subclavian aneurysm	Innominate and carotid	Subclavian	104th day	Suppuration and hemorrhage, 2d operation
30	Subclavian aneurysm	Innominate, carotid, subclavian	33d day	Hemorrhage
31	Subclavian aneurysm	Innominate pressure	17th day	Hemorrhage
32	Subclavian aneurysm	Innominate, carotid, subclavian	2d day	Cerebral embolus and thrombosis
33	Subclavian aneurysm	Innominate	18th day	Suppuration and hemorrhage
34	Subclavian aneurysm	Innominate, carotid, vertebral	16th day	Left cerebral embolus
35	Subclavian aneurysm	Innominate and carotid	18 hours	Cerebral thrombosis
37	Subclavian aneurysm	Innominate and carotid	10th day	Suppuration and bronchopneumonia
38	Subclavian aneurysm	Attempted innominate	16th day	Suppuration and hemorrhage
41	Bifurcation.....	Attempted innominate	17 hours	Shock
43	Subclavian aneurysm	Innominate	104th day	Cardiac failure
44	Wound.....	Carotid	Innominate, carotid, subclavian	Hour	Shock
45	Subclavian aneurysm	Innominate	Carotid	41st day	Suppuration and hemorrhage
46	Carotid aneurysm....	Innominate	9th day	Cerebral lesion
47	Subclavian.....	Subclavian	Innominate and carotid	1 hour	Shock, rupture, second aneurysm
48	Bifurcation aneurysm	Innominate	3d day	Hemorrhage
50	Bifurcation aneurysm	Innominate	Carotid and vertebral	18th day	Shock of second operation
51	Subclavian aneurysm	Innominate and subclavian	Hour	Shock

beneficial result on the aneurysm. I have regretted that owing to lack of experience I used this procedure for exposure rather than resection.

Silk or hemp was the original ligature material. From 1880 to 1900 many experiments were being conducted on ligature material. One reads of the advantages and disadvantages of absorbable and non-absorbable materials, or of the various substances in each class. Ox aorta, ox peritoneum or gold beater's skin, kangaroo tendon, carbolized catgut, chromic catgut, horse hair, silver wire and many other substances were used. Ballance and Edmunds, in an exhaustive study on ligations, came to the conclusion that an aseptic ligature which remained sufficiently long to cause permanent occlusion was the best. Heavy

TABLE 10—Deaths Occurring Following Ligations—Continued

No	Diagnosis	First Ligation	Second Ligation	Date	Cause of Death
52	Bifurcation aneurysm	Innominate and carotid		26 hours	Hemiplegia, carotid, thrombosis
53	Wound	Innominate			
59	Subclavian aneurysm	Innominate		4th day	Bronchopneumonia
62	Subclavian aneurysm	Innominate and carotid	Carotid	1 month	Suppuration and hem- orrhage, 2d operation
65	Bifurcation aneurysm	Innominate		20 hours	Shock
72	Subclavian aneurysm	Innominate		67th day	Suppuration and hem- orrhage
75	Bifurcation aneurysm	Innominate and carotid		1th day	Hemiplegia
78		Attempted in- nominate			Innominate rupture, hemorrhage
79	Wound	Innominate pressure; subclavian		3 hours	Shock
81	Wound	Innominate suture		5th day	Mediastinitis
83	Innominate aneurysm	Attempted in- nominate			Shock
SUMMARY					
Suppuration and hemorrhage					12
Shock					11
Hemorrhage					10
Suppuration and other conditions					8
Cerebral lesion					7
Miscellaneous					4
Unknown					2

skill, kangaroo tendon and modern chromicized gut fill these conditions and the latter is now provided with so little variation that it has become the ligature of choice.

These authors also showed that a force sufficient to occlude without rupture insured the best results. They advise for this a force of between 3 and 10 pounds, for the innominate artery, and a knot which they devised and which they called the stay knot (fig 5). Two ligatures are placed side by side and the first knot tied independently but with the strands parallel throughout. The second knot is tied with both strands together in such a way as to form a square knot for each strand. The advantage of this procedure is that the friction between the two strands prevents slipping while tying the second knot. This makes it possible to apply the correct force to the first knot and to have it remain con-

stant. When the coats are crushed there is devitalized tissue which is accepted in modern theory to be *favorable to infection*. When infection starts at the site of ligation, the picture of ulceration of the vessel and hemorrhage is almost constant.

Drainage was constant in the preaseptic period and is mentioned in 8 of 10 cases in the period from 1880 to 1900, and in 9 of 15 cases

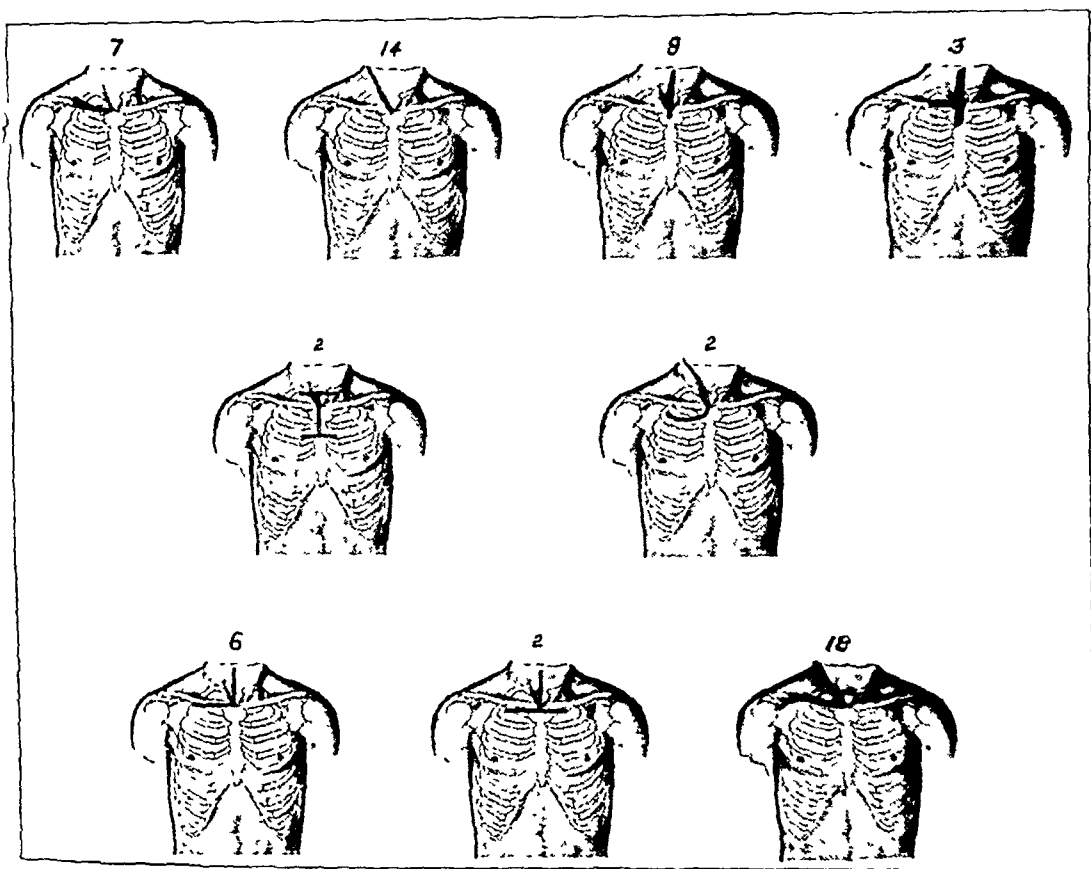


Fig. 3.—Diagram of incisions used in operations on the innominate artery. The figures show the number of times each type of incision was used.

since 1900. Surgeons are gradually draining fewer and fewer operative wounds and are profiting by the decrease in infection.

The advisability of associated ligation of other vessels is difficult to work out from the statistics of this series. In most of the cases before asepsis, the innominate alone was ligated. Whether the improvement since then can be attributed to more extensive ligation is difficult to say.

Figure 1 shows that the mortality in ligations of the innominate artery is 65 per cent; of the innominate and carotid, 45 per cent; of the innominate, carotid and subclavian, 33 per cent; of the innominate and subclavian, 25 per cent, and of the innominate, carotid and vertebral, 100 per cent; also that previous or subsequent ligations were done respectively in the innominate in 30 per cent; the innominate and carotid, 30 per cent; the innominate, carotid and subclavian, 16.66 per cent; the innominate and subclavian, 0 per cent, and in the innominate, carotid and vertebral, 0 per cent. The aneurysm was benefited respectively in the innominate, 58 per cent; the innominate and carotid, 66 per cent; the innominate, carotid and subclavian, 80 per cent; the

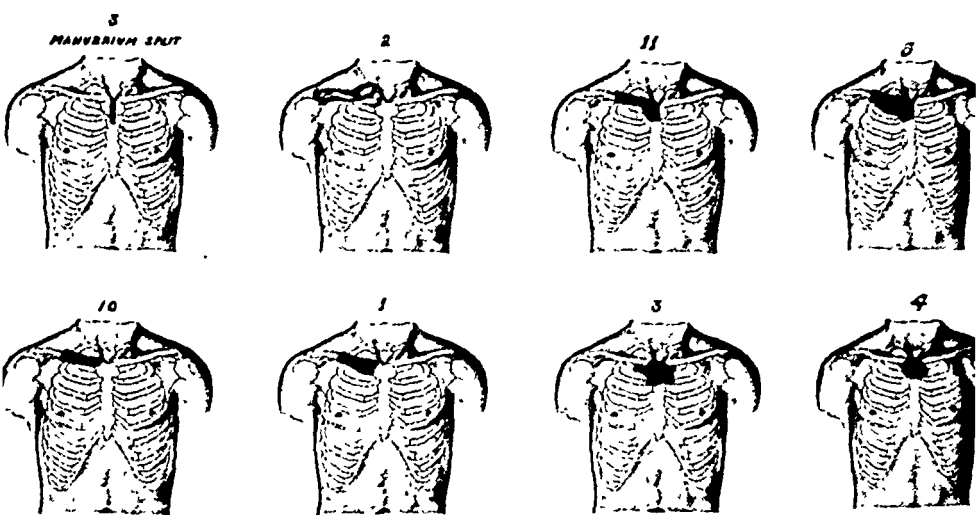


Fig. 4.—Diagram of bone resection in operations on the innominate artery. The figures show the number of times each type of bone resection was done.

innominate and subclavian, 75 per cent; the innominate, carotid and vertebral, 0 per cent. These figures would indicate that multiple ligation is advisable; that combinations including the subclavian are better than those including the carotid, and that the vertebral should not be included.

It has been argued that the carotid should be ligated with the innominate, as the collateral for the subclavian is largely retrograde from the brain to the arm. The 7 cases of cerebral lesion occurring in the series do not seem to bear out this assertion as 4 occurred in ligations of the innominate and carotid arteries, 1 in ligation of the innominate, 1 in ligations of the innominate, carotid and vertebral and 1 in

ligations of the innominate, carotid and subclavian. Of the 7 cases, 6 were associated with ligation of the carotid.

It is possible that with the subclavian tied there is a better chance of protecting the cerebral circulation than with ligation of the carotid, and certainly the incidence of thrombosis is reduced.

If the ligation of the innominate is proximal to an aneurysm, distal ligation of the carotid or subclavian and extirpation of the sac, if possible, is the best operation for cure of the aneurysm. As 56 of the 75 aneurysms involved the subclavian and 15 involved the bifurcation or

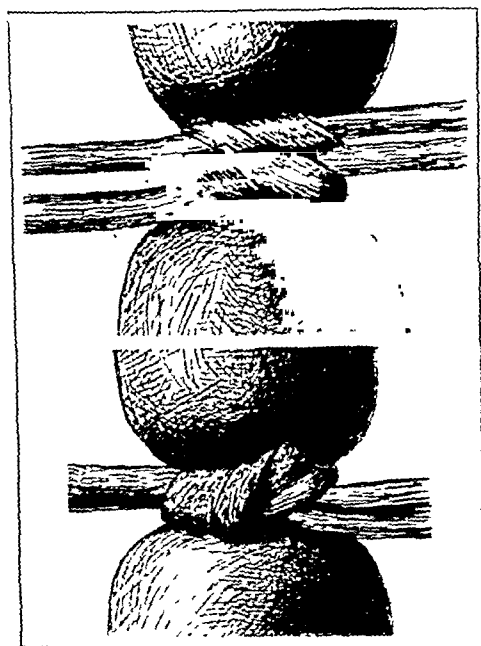


Fig. 5.—Ballance and Edmunds' stay knot.

the innominate as opposed to 8 involving the carotid, distal ligation of the subclavian would occur many more times.

There were 15 cases of proximal and distal ligation, 7 of which were done in two stages, and in 7 the sac was partially or wholly extirpated. The results showed 12 cures, 1 case in which there was no improvement and 2 deaths (table 11). This is by far the best showing in the series.

The most advisable operation from all these data would be multiple ligation, proximal and distal to the aneurysm, if possible, and with a preference for ligating the subclavian rather than the carotid artery.

The innominate was severed between ligatures in 3 cases, in 2 of which the patients recovered. This is too meager information from

which to form conclusions, but added to this there is experimental work indicating better results when the artery is cut. Horsley showed that the cut ends immediately retract. This increases the thickness of the vessel wall. The raw exposed end gets more fibroblasts from the sur-

TABLE 11.—*Proximal and Distal Ligations*

No.	Diagnosis	First Operation	Second Operation	Result	Date	Cause of Death	Aneurysm
47	Subclavian aneurysm	Subclavian ligation, excision of sac	Innominate ligation	Death	1 hour	Shock	Second ruptured
51	Subclavian aneurysm	Innominate, subclavian ligation; sac partly excised	Death	Hour	Shock	
54	Subclavian aneurysm	Innominate and carotid ligation	Subclavian ligation	Recovery	9 months	Cured
55	Carotid aneurysm	Innominate ligation	Carotid ligation; excision of sac	Recovery	9 months	Cured
56	Subclavian aneurysm	Innominate ligated and cut	Subclavian ligation; excision of sac	Recovery	7 months	Cured
57	Subclavian aneurysm	Partial innominate ligation	Subclavian ligation	Recovery	15 years	Cured
63	Subclavian aneurysm	Innominate, carotid, subclavian and jugular vein ligation	Recovery	4 months	Cured
64	Bifurcation aneurysm	Innominate, carotid, subclavian ligation; excision of sac	Recovery	17 months	Cured
70	Subclavian aneurysm	Subclavian	Innominate	Recovery	13 months	Improved
80	Subclavian aneurysm	Innominate and subclavian artery and vein ligation; excision of sac	Recovery	12th day	Cured
82	Carotid aneurysm	Innominate ligation	Carotid ligation	Recovery	4 years	Cured
86	Carotid aneurysm	Innominate, carotid, subclavian ligation; excision of sac	Recovery	6 years	Cured
88	Subclavian aneurysm	Innominate and subclavian artery and vein ligation; sac sutured	Recovery	1 year	Cured
89	Bifurcation aneurysm	Innominate, carotid and subclavian ligation	Recovery	19 months	Cured
91	Bifurcation aneurysm	Innominate and subclavian ligation; sac packed	Recovery	6 months	Cured

rounding tissue and cicatrizes more rapidly. If the artery is to be severed, it is advisable to apply 3 ligatures and to cut between the two distal ones. The end of the artery is then at rest because of the proximal ligature and can heal better.

Another argument in favor of severing the artery was brought forward by Leriche at the 1922 Congress of Surgeons. The vasocon-

strictor fibers running along the great vessels are only temporarily injured by ligation in continuity. They are destroyed by cutting, and the periphery therefore gets better circulation. This may be shown by tying and cutting the femoral artery. In one minute there is a flow from the distal end which in five minutes begins to pulsate. This is due to the dilatation of the anastomosing arterioles, particularly in the muscles.

Associated with the problem of severing the artery is the problem of ligation of the accompanying vein. Makins, Leriche, Brooks and Martin, Drummond and others, have shown that the peripheral circulation is improved by ligating the vein at the site of the arterial ligation, or better at a proximal point. In a series of experiments on rabbits, Brooks and Martin showed that ligation of the common or external iliac artery caused gangrene in 71.5 per cent of a series, while simultaneous ligation of the common iliac vein caused gangrene in only 33.3 per cent. The same tendency has been shown by Drummond in ligation of the mesenteric vessels. Holman quoted a series collected by Heidrich, in which gangrene developed in 15.4 per cent of 995 arterial ligations and in only 8.5 per cent of 198 arterial and venous ligations.

In ligations of the innominate there are two peripheral circulations to consider; one is that of the subclavian and the other that of the carotid. In the subclavian areas, i. e., the upper extremity, no cases of gangrene have been reported, although there are some cases of atrophy which might be considered the chronic result of anemia in which gangrene is the acute. In the 75 ligations there have been 7 cases of death from cerebral lesions. Some of these must be attributed to anemia. Ligation of the innominate vein would help the upper extremity according to the experimental work. In the case of the brain, however, the circulation differs. Here there is a right and left supply, and right and left return. Both anastomose widely, the arterial side through the circle of Willis, the venous side through the dural sinuses. Obstruction to the venous return by ligating the right innominate vein might, by increasing the resistance to outflow, increase the cerebral circulation, but without experimental data one can only theorize. At least the evidence at present is in favor of ligation of the vein.

If ligation of the innominate is contemplated, it should be done early. The operation is easier in the early stages of a vascular lesion than after marked pathologic process has developed. An operation in which the mortality in the last 25 cases was 16 per cent is certainly a justifiable procedure since the pathologic process which indicates it is of such a serious nature.

ABSTRACT OF CASES

CASE 1² (surgeon, V. Mott, 1818).—A white man, aged 57, was admitted to the New York Hospital, on March 1, 1818, with catarrh and swelling of the right arm and shoulder. He had fallen one week before admission, and two days later had noticed pain in the shoulder. Under medical treatment, his general condition improved and the swelling subsided in the arm and neck, leaving a definite tumor which showed faint pulsation. On May 3, something gave way in the tumor. It increased one-third in size, and pulsation became distinctly perceptible. By May 10, it measured 4 by $5\frac{1}{4}$ inches (10.2 by 13.3 cm.). The arm was useless and painful, and the patient asked for an operation.

On May 11, with the patient under 70 minims of tincture of opium, an incision 3 inches (7.6 cm.) long was made above the clavicle and a second one along the medial border of the right sternomastoid. The sternal portion of this muscle was cut, and the carotid and subclavian arteries were exposed. The latter was unhealthy. The innominate artery was dissected out bluntly. A silk ligature passed from below upward was tied around the artery $\frac{1}{2}$ inch from the bifurcation. It was gradually drawn tight, causing no change in the heart or the lungs, but stopping the circulation in the temporal and radial arteries. The second knot was tied. The tumor immediately decreased one-third in size. The wound was closed about the ligature. The operation lasted one hour.

After operation, the patient was comfortable. The pulse rate was 69 and the right arm was slightly cooler than the left. The arm was wrapped in absorbent cotton. That evening the patient had a slight headache and was bled 16 ounces (473.1 cc.). On the third day, there was foul suppuration through the dressing. On the fourth day, the wound was dressed. There was healthy suppuration. The wound was united almost to the angle. There was less discharge and less odor on the eighth day; the tumor decreased two-thirds. A small slough was seen in the dressing. A hemorrhage filled the wound, but was easily stopped by pressure. On the eleventh day, the slough came away from the bottom of the wound. On the thirteenth day, the patient was weaker; the large ligature came away. On the fifteenth day, he was up and walking, and on the nineteenth day he went up two flights of stairs. On the twenty-second day, there was a hemorrhage of 24 ounces (710 cc.). The pulse ceased, but gradually recovered. On the twenty-third day, the patient was vomiting and sick. There was a foul discharge, and a hemorrhage of 4 ounces (118.4 cc.). On the twenty-fifth day, the patient died after a hemorrhage of 8 ounces (236 cc.).

Autopsy showed suppuration of the wound. The innominate artery was inflamed, and the ligature had cut through the vessel. The carotid was blocked. The subclavian was pervious and opened directly into the ulcer which was at its origin. A diseased opening in this artery communicated with the sac.

CASE 2³ (surgeon, Graefe, 1822).—A sailor, aged 30, was admitted to the hospital in 1821, with a subclavian aneurysm of rapid growth. On March 15, 1822, an incision was made along the anterior edge of the sternomastoid, exposing the carotid artery. This was followed down to the innominate artery. The ligature was passed 1 inch from the aorta and tied.

2. Mott, V.: Reflections on Securing in a Ligature the Arteria Innominata, *Med. & Surg. Reg.* 1:9, 1818; Further Remarks on the Case of Ligature of the Arteria Innominata, *ibid.* 1:2, 1820; A Case in Which the Innominate Artery was Tied by a Surgical Operation, *Am. Med. Recorder* 2:374, 1819.

3. Wagner: Ligature of the Innominate Artery, *Med. & Physical J.* 49:475, 1823. Sheen: On Ligature of the Innominate Artery, *Ann. Surg.* 42:1, 1905.

The ligature came away fourteen days after operation, with part of the bifurcation of the artery. There was suppuration. Hemorrhage, which occurred some time afterward, was controlled by pressure. The patient complained of pain in the tumor. Fluctuation could be felt. The sac was incised, and pus and blood drained out. The old wound healed; the new wound drained. There were hemoptysis, fever, vomiting and suppuration. The patient died on the sixty-seventh day.

Autopsy showed lung disease. The innominate artery was closed by a clot on the cardiac side. Ample anastomosis was proved by injection. The hemorrhages apparently were distal.

CASE 3¹ (surgeon, Norman, 1824).—A man with a tumor of the subclavian artery underwent an emergency operation, the innominate artery being ligated. He died on the fifth day after operation, showing acute pericarditis. The ligature was in good condition with no pus and a firm clot on the cardiac side.

CASE 4⁵ (surgeon, Arcndt, 1827).—A man, aged 36, was admitted to the hospital on Dec. 3, 1827, with his right arm painful, swollen and inflamed. There was a swelling the size of a goose egg, pulsating, behind the right clavicle. He had received a blow on the shoulder one year before.

On December 24, an incision $3\frac{1}{2}$ inches (8.9 cm.) long was made along the inner border of the right sternomastoid. The trachea was followed down to the innominate artery. The needle was broken on the first passage of the ligature, but the second time it was successful, and the artery was tied. Pulsation in the aneurysm, subclavian and carotid, ceased at once.

After the operation, the arm was cool and dark blue. The patient was flushed and anxious, and complained of pain under the sternum. The pulse rate was 148. The patient was bled 20 ounces (591.5 cc.). On the first day after operation the arm was warmer, but swollen, numb and painful. On the second day the temperature was higher, and the pulse rate was 145, and dyspnea and hoarseness developed. The arm was less swollen. The patient was bled 10 ounces (295.7 cc.). On the fourth day thin pus came from the wound. Considerable pus was noted until the eighth day, when the patient died from exhaustion.

At autopsy considerable infection of the wound and surrounding tissue was noted. There was pneumonia in the right lung and serous pleurisy. The subclavian artery was inflamed. The innominate ligature was tight and had cut through the coats. The carotid and subclavian arteries had collapsed. There was edema of the brain and enlargement and softening of the liver.

CASE 5⁶ (surgeon, Hall, 1830).—A white man, aged 52, was admitted to the hospital on Sept. 4, 1830. For seven months he had had a pulsating tumor above the right clavicle. There were loss of power and edema in the right arm, and some difficulty in respiration and swallowing. For three days he was bled 1 pint a day.

Operation was performed on September 7 with the patient in a sitting position. A midline incision was made from the thyroid body to the sternum and transversely from there to the sternomastoid. There were many diseased glands. The innominate artery was dissected out easily with the finger. It was found to be diseased

4. Polland: Statistics of Subclavian Aneurysm, *Guy's Hosp. Rep.* **17**:126, 1872. Gore: Ligature of the Innominate Artery for Subclavian Aneurysm, *Lancet* **2**:119, 1878.

5. Polland (footnote 4, first reference).

6. Hall: Case of Aneurysm of the Right Subclavian Artery in Which Ligature was Applied to the Arteria Innominata, *Baltimore M. & S. J.* **1**:125, 1833.

and dilated. As the finger was withdrawn, there was a slight flow of blood which became copious without pulsation. A ligature was passed around the innominate artery and tied. During application the hemorrhage ceased, but after it was tied it began again. The wound was packed with sponges. The wound was closed over this with sutures, and the hemorrhage stopped. The patient was in a poor condition.

Pulsations in the carotid and subclavian arteries were hardly present for two hours after operation. They returned to normal within the first day. Two days after operation, the patient was bled 15 ounces (444 cc.). Four days after, he was up and around and insisted on going home. There was a sudden change in the evening; the pulse rate was 134, and there were dyspnea, fever, a slight discharge from the wound and pain about the sternum. The patient died early the next morning.

At autopsy the wound was found to be badly infected. There was pericarditis. There were diseased glands along the trachea and all the great vessels were diseased. Infection and softening of the innominate and carotid arteries were noted. The ligature had been passed through the innominate, but not around it. The aneurysm contained a clot.

CASE 6⁷ (surgeon, W. H. Porter, 1831).—A man, aged 47, was admitted to the hospital on Dec. 6, 1831, with a large pulsating tumor filling almost the entire right side of the neck. It measured $5\frac{3}{4}$ by 3 inches. There was severe pain in the tumor, and pain and numbness in the forearm and hand. No pulse was felt at the wrist or elbow. The hand was cold and bluish. The mass was first noticed two and one-half years ago; the pain and numbness, one year ago. The patient was treated medically for five days without improvement.

On December 10, an incision 2 inches (5 cm.) long was made from the left sternoclavicular joint to just above the head of the right clavicle, and was carried upward from its left extremity. The right sternomastoid muscle was divided. The sternohyoid and thyroid were cut. The carotid artery was anterior and was found in this region. An attempt was made to dissect the innominate with the finger. Anteriorly, this was difficult because of the sternum and the struggling and crying of the patient. On the right side there seemed to be an enormous pulsating sac. The limits on the right side could not be reached. Compression of the innominate stopped all pulsation in the vessel. After one hour and fifteen minutes the operation was abandoned, and the wound was closed with two sutures.

The patient had a chill two hours after operation. Fever developed that night. He was bled 22 ounces (650 cc.). One day after operation the pulsation seemed diminished, and the pain and numbness were gone. Two days after there were a red serous discharge from the wound and some cough. On the third day there was still some discharge, but the cough was better. On the fourth day the inflammation of the wound was gone, and there was less pulsation. On the fifth day pulsation returned in the tumor; the arm felt cold to the patient, although it was hot and dry. On the sixteenth day the wound was almost healed; the tumor was harder, firmer and probably smaller. Two months after, the tumor was one-fourth the size that it was on admission; the arm was almost normal, and the patient's health much better.

CASE 7⁸ (surgeon, W. Bland, 1832).—A man, aged 31, had noticed a small throbbing tumor above the right clavicle for two years. He had had pain and numbness of the right arm. On admission to the hospital, a throbbing tumor the

7. Porter, W. H.: Case of Aneurysm, Dublin J. M. & Chem. Sc. 1:25, 1832.

8. Bland: Operation of Tying the Arteria Innominata, Lancet 1:97, 1832.

size of a pigeon's egg was found. Despite two bleedings six months before and rest, the tumor had increased gradually in size and the patient's general health became worse. His pulse rate was from 100 to 104 until the day before admission, and then it dropped to 60 and became irregular and intermittent. A terrific pain developed in the left side.

On March 28, 1832, a vertical incision was made 2 inches long and 1 inch from the upper margin of the sternum. The sternomastoid was cut, and the sternothyroid and sternohyoid were split. The innominate was found with the finger and isolated. An aneurysm needle was passed; then a ligature of two sutures was tied firmly enough to cut the inner coat.

After operation the pulse rate varied from 130 to 140. The patient was having no pain. On the second day the right arm was as warm as the left. The tumor subsided rapidly, and the numbness was almost gone. The pulse rate varied from 126 to 138. When the wound was dressed on the third day after operation it was healthy. The tumor was reduced one-third. The patient had good use of both hands. No pulsation was felt in any branches. The patient's condition progressed until the eighth day; the pulse rate was gradually dropping, when he noticed slight numbness returning in the right hand. On the tenth day, the wound was filling in. The pus was less creamy. A slight headache occurred in the afternoon. The tumor measured from 3 to 4 inches at that time. On the fifteenth day, the pulse rate was elevated; the patient had a sore throat and experienced some difficulty in swallowing. The discharge was scanty. There was some fever. The wound was nearly closed. On the sixteenth day, the discharge became bloody. The throat was tender and painful. On the seventeenth day there was a hemorrhage of 4 or 5 ounces (118 or 148 cc.). Early in the morning of that day, the patient felt better. In the afternoon there was a few ounces of blood from the wound, and the tumor increased in size. A director was passed down to the ligature, but there was no hemorrhage. Early on the eighteenth day, there was a hemorrhage of from 10 to 12 ounces (296 or 355 cc.). The pulse became weak; the right arm became cold, and patient died at 7 a. m.

At autopsy the pleura was found to be normal. An ounce of pus was found at the base of the wound. The ligature had almost divided the artery. The innominate and carotid arteries were solid with clot; the subclavian artery was open, and the hemorrhage probably came from this point.

CASE 8^o (surgeon, Bujalsky, 1833).—A man, aged 56, was admitted to the hospital with an aneurysm of the right subclavian artery extending from the axilla to the inferior maxilla. The skin over it was red.

On March 11, 1833, an incision was made over the tumor to the inner margin of the sternomastoid. The operation was difficult owing to old gland scars. The innominate was tied with a "tourniquet." Chills, fever and a rapid pulse developed. Death occurred on the fifth day.

Autopsy showed aneurysmal dilatation of the heart and the aorta; there was pus in the pericardium and the pleura.

CASE 9th (surgeon, Unknown, 1834?).—The history in this case is unknown. The innominate artery was ligated, and the patient died of hemorrhage.

CASE 10th (surgeon, Kuhl, 1836).—A woman, aged 43, had a malignant new growth involving both sides of the forehead. The tumor was vascular, and ligation was done as preparation for operation. An attempt was made to ligate the innomi-

9. Sheen: On Ligation of the Innominate Artery, *Ann. Surg.* 42:1, 1905.

10. Dupuytren: *Leçons orales de clinique chirurgicale*, Paris, 1834, vol. 4, p. 611.

11. Pollard (footnote 4, first reference, p. 86).

nate artery, but the carotid and subclavian arteries were ligated together in one ligature $\frac{3}{4}$ inch above the bifurcation. The patient was unconscious for four hours following the operation. The pulse in the right arm and right side of the head ceased. She became conscious after this, but she had difficulty in breathing and swallowing, and died on the third day.

Autopsy showed a rupture of the coats of the arteries and the canals obstructed.

CASE 11¹² (surgeon, Lizar, 1837).—A white man, aged 30, was admitted to the hospital on May 28, 1837, fifteen months after a fall on the right elbow. From five to six weeks before admission, pain appeared in the right forearm and arm. No tumor had been noticed. Examination showed a pulsating tumor the size of a small egg above and medial to the clavicle. There were anesthesia and tingling in the fingers.

On May 31, an incision was made 1 inch above the sternum and 4 inches in length along the margin of the sternomastoid. The sternohyoid and sternothyroid muscles were divided. The carotid and innominate arteries were exposed. The latter were cleaned. An aneurysm needle was carried around it from the right side inward toward the trachea. The vessel was compressed, and pulsation in the tumor, the carotid and the subclavian arteries ceased. The artery was tied, and as this was done the patient complained bitterly of pain in his heart. The skin was brought together with four sutures. The operation lasted fifteen minutes.

Two hours after operation, the right side of the face was shriveled and cold. There was little difference in the two arms, except that there was no pulse in the right radial or right temporal arteries. There was pain in the course of the carotid and brachial arteries and in the back of the arm. Numbness and tingling were noted in the fingers. The left carotid was beating violently. Four hours after operation, pain was felt in the right side of the chest on deep breathing. Headache was present, but there was no pulsation. Ten hours after, the headache was worse, and there was a sensation of suffocation. On the first day, a slight pulsation was felt in the temporal artery. The patient progressed well. On the second day, he had no pain. The radial pulse was weak. The wound looked as if there would be two-thirds primary union. On the fourth day, the pulse was felt in the radial and temporal arteries, but not in the tumor. On the ninth day, there was considerable thick pus from the wound. Slight nausea occurred on the twelfth day. The patient vomited a large amount of bilious material. On the fifteenth day, the wound healed except for a small sinus which was discharging healthy pus. On the sixteenth day, the knot of the ligature was found on the dressing. On the nineteenth day, a severe, dry cough developed. A hemorrhage of 8 ounces occurred from the wound, which was stopped by pressure. The patient was bled by vein of 20 ounces. On the twentieth day, there was hemorrhage of 4 ounces, and on the twenty-first day one of from 2 to 3 ounces (59 to 89 cc.), which was stopped by lint. Evidently there was an internal hemorrhage. Cough and dyspnea developed; the patient spit blood. Death occurred at 1:30 a. m.

Autopsy showed that the innominate artery was filled with a dense clot from origin to ligation. The right common carotid was entirely clotted; the thyroid artery, internal mammary, transverse cervical, vertebral and subclavian arteries were pervious, the latter from its origin to the tumor. The aneurysm of the subclavian artery beyond this point was collapsed and contained clot. The fatal hemorrhage was apparently from the vertebral artery into the pleura, which contained 20 ounces.

12. Lizar: Aneurysm of the Subclavian Artery Treated by Ligature of the Arteria Innominate, *Lancet* 2:445 and 602, 1836. Edinensis: Mr. Lizar's Case of Ligature of the Arteria Innominate, *Lancet* 1:466, 1837.

CASE 12¹³ (surgeon, Hoffman, 1839).—A negro, aged 63, had a subclavian aneurysm of five months' duration. The base was 5 inches (12.7 cm.) around and extended chiefly below the clavicle.

On Oct. 26, 1839, an attempt was made to ligate the subclavian or the innominate arteries. The vessels and the aneurysm were exposed. Both vessels were too much diseased to be ligated. The patient died on Jan. 19, 1840, from exhaustion.

Autopsy showed two aneurysms of the subclavian artery, the first one measuring 1 inch, the second 6 inches (15.2 cm.) in diameter. The innominate and aorta were atheromatous, the former slightly dilated.

CASE 13¹⁴ (surgeon, Hutin, 1841).—In a fight between two soldiers with scissors, on Oct. 28, 1841, one of them, aged 30, was wounded in the right axilla. He had a sharp hemorrhage and was brought to the hospital. The next day a wound, 6 mm. in length and 2 mm. wide, filled with clot, was present in the middle of the axilla. Four hemorrhages occurred in the next ten days, all stopping of their own accord. On November 9, owing to sudden severe pain, the wound was dressed and there was a severe hemorrhage. This was stopped by pressure on the subclavian or pressure in the wound. The pulsation in the arm stopped, as did doubly ligated, and the wound closed. The third portion of the subclavian was the hemorrhages. The patient improved for five days. He was up on the sixth day, and when attempting to defecate had a severe hemorrhage. Two more hemorrhages occurred on the following two days. On the eighteenth day, a ligature surrounded by pus was in the dressing, and there was a very severe hemorrhage. Three more severe hemorrhages occurred that day.

Operation was performed on November 27, the patient struggling throughout. The innominate artery was finally isolated and four threads in a band were placed around it. Another precautionary ligature was placed. The patient died twelve hours after operation.

Autopsy showed that the original wounded artery was the inferior thoracic. The subclavian was obliterated but had ruptured proximally at the site of the ligature. The middle and internal coats had been cut through. The ligature of the innominate artery was all right. The patient died of shock preceded by hemorrhage and operation.

CASE 14¹⁵ (surgeon, Key, 1844).—A woman, aged 46, was admitted to Guy's Hospital on April 25, 1844, with a pulsating tumor the size of a pigeon's egg, above the right clavicle, of three months' duration. Pain was felt in the right arm. The pulses were equal, and the heart sounds were natural.

In April, 1844, an incision was made along the clavicle and sternomastoid. The sternomastoid was cut. The aneurysm was behind the subclavian artery preventing a passage of the needle. An attempt was made to ligate the innominate. This had to be given up. The operation lasted one hour.

13. Pollard: Statistics on Subclavian Aneurysm, Guy's Hosp. Rep. **16**:71, 1871.
Norris: Contributions to Practical Surgery, Philadelphia, Lindsay and Blakeston, 1873, p. 284.

14. Hutin: Wound by Sharp Instrument in the Axilla; Ligature of the Subclavian, Hemorrhage; Ligature of the Innominate; Death, Ann. de la Chir. Française et Étrangère **4**:5, 1842; abstr., Lancet **2**:230, 1841.

15. Physical Soc. of Guy's Hosp., Lond. Med. Gaz. **35**:334, 1844-1845. Crisp: Structure Diseases and Injuries of the Blood Vessels, London, 1847, p. 206.
Pollard (footnote 13, p. 70).

Pulsation in the sac disappeared on the second day after operation. On the seventh day, a venous hemorrhage occurred. By the eighteenth day, the sac had increased, and there was much pain in the right arm. On the twenty-third day, the patient died from pressure on the trachea.

Autopsy showed that the aorta contained atheromatous deposits, and there was a small aneurysm in the thoracic portion. The carotid was healthy. The aneurysm was of the upper part of the innominate artery and origin of subclavian pressing on the right bronchus. The aneurysmal sac contained a firm clot. Death was due to pressure on the trachea.

CASE 15¹⁰ (surgeon, Peixoto, 1851).—A physician, aged 33, nineteen years before had an erectile tumor of the right ear. The posterior auricular artery was ligated by Nelaton six years before. When the ligature fell, there was a severe hemorrhage, and several abnormal branches were ligated. The tumor recurred just before admission. On Nov. 14, 1851, the common carotid artery was ligated in the neck. The ligature was brought out through the wound. The blood supply of the tumor was shut off by this. The patient lost 5 or 6 ounces (148 or 178 cc.) of blood two or three times during a fortnight. On November 27, a chain ligature was applied about the ear. There was suppuration and the tumor became gangrenous, finally healing over with skin. On December 4, there was a slight hemorrhage from the carotid. The next day, a ligature was applied to the carotid above and below the old ligature. On December 6, two small hemorrhages occurred. On December 7, the patient tore off the dressings. There was an arterial hemorrhage of 5 ounces of blood in the evening, and the pulsations of the carotid below the ligature became sensible. On December 8, at 6 a. m. the suture points ruptured, and there was a sharp hemorrhage of half a pint.

On December 8, an incision was made along the inner border of the sternothyroid. The innominate artery was brought out by blunt dissection. A ligature was passed around it. With this in place, the old wound was opened and the clots cleaned out. The carotid ligature came away. There was no recurrence of hemorrhage. Therefore, the innominate ligature was left in place without tightening.

There was considerable cough for twenty-four hours after operation, but this cleared up. The upper wound suppurated at once. On the tenth day, both were suppurating, but the general condition was better. On the thirteenth day, the innominate ligature was withdrawn. The patient progressed to a cure in two months. Velpeau stated that there is no proof that this was the innominate artery. If it was the innominate artery, the ligature was never tightened, and although the observation was made that there was a clot in this artery, obliteration cannot be accepted as proved.

CASE 16¹¹ (surgeon, Pirogoff, 1852).—A man, aged 46, complained of a mass the size of a pigeon's egg in the right supraclavicular region at the site of an old abscess. The pulse at the wrists was unequal. The entire arm was painful. A diagnosis of aneurysm of the right subclavian was made.

A median line incision was made in the suprasternal fossa. The innominate was exposed and ligated.

16. Velpeau: Report on Observation of Peixoto, *Bull. Acad. de méd.* **19**:452, 1853. Peixoto: Observations on the Ligature of the Innominate, *Mém. de l'Acad. Imp. de méd.* **19**:23, 1855; Case of Successful Ligature of the Arteria Innominate, *Brit. & Foreign Med.-Chir. Rev.* **18**:275, 1856; abstr., *Am. J. M. Sc.* **33**:255, 1857.

17. Pirogoff: *Grundzüge der allgemeinen Kriegs Chirurgie*, 1864, pt. 1, p. 459.

After operation the tension and pulsation decreased immediately. At the end of twenty-four hours there was severe infection of the arterial sheath. Facial paralysis developed. The patient died from mediastinitis and pericarditis in forty-eight hours.

Autopsy showed suppuration at the ligature, pleurisy, purulent mediastinitis and pneumonia. There was blood over both hemispheres of the brain. The aneurysm was of the subclavian artery.

CASE 17¹⁸ (surgeon, Gore, 1856).—A man, aged 52, was admitted to the Bath Hospital on Sept. 22, 1856. He had noticed a swelling in the right axilla the size of a walnut three years before. This increased in size for a few weeks, and there was pain down to the elbow. It then remained the same until six months before the patient was admitted to the hospital, when it began to enlarge rapidly and the pain began to increase. On admission a pulsating tumor filled the axilla and extended up to the clavicle and scalene muscles. He was having intense pain.

On September 24, with the patient under chloroform, an incision was made a little above the inner end of the clavicle and along the border of the sternomastoid. The sternomastoid, sternohyoid and sternothyroid were cut. The innominate artery was exposed and tied with a hemp ligature passed behind from the outside. The pulse ceased in the tumor, the face and the arm. The limb was wrapped in absorbent cotton.

On the first day after operation, there was no pain. There was no pulse in the right arm or in the head, except a faint pulse in the temporal region. On the fourth day, chill and cough developed; the wound was red and discharging. The three sutures were removed. On the eleventh day, the patient had more chills. There was tension in the arm and in the tumor. On the fourteenth day, the wound was cleaner, but pulsation was noticed in the ligature. On the sixteenth day, hemorrhage occurred which lasted an hour, and was followed by death.

Autopsy showed the ligature attached to the innominate artery and partly cut through. The cardiac end was partially clogged by a firm clot. The aneurysm was small and contained a firm clot which extended to the subclavian, axillary and brachial arteries. The carotid was clotted to the bifurcation. In the anterior mediastinum there was a large cavity containing foul pus.

CASE 18¹⁹ (surgeon, Cooper, 1859).—The patient had an aneurysm of the right carotid and subclavian arteries.

In March, 1859, an incision, 4 inches long, was made parallel to, and $\frac{1}{2}$ inch above, the upper margin of the clavicle, running from inside the sternoclavicular joint to the margin of the trapezius, and joined at the middle by a vertical one. The tumor was exposed, and was found to extend beneath the clavicle. The sternal extremity of the clavicle and the top of the sternum were removed. The innominate artery was barely exposed. One third of the artery was dilated. Ligation was done $\frac{3}{4}$ inch (1.9 cm.) from the aorta.

The patient was all right for five days after operation. He sank and became restless after this. There was suppression of urine. Death occurred on the ninth day.

Autopsy showed the right side of the heart slightly dilated and pus in the right kidney. There were two aneurysms adherent to each other, one of the subclavian and one of the carotid artery.

18. Gore (footnote 4, second reference).

19. Cooper: Aneurysm of Right Carotid and Subclavian Arteries; Ligation of Arteria Innominate, *Am. J. M. Sc.* 38:395, 1859; *Ligature du tronc brachiocephalique*, *Gaz. hebdomadaire de med.* 8:612, 1861.

CASE 19²⁰ (surgeon, Cooper, 1860).—A man, aged 31, was admitted to the hospital on Sept. 23, 1860, with aneurysm of the right subclavian artery of four months' duration. He was in good condition. There was a large pulsating mass filling the supraclavicular triangle.

On September 24, a crucial incision, 5 inches long, was made with its center on the tumor. The flaps were turned back in all directions. The aneurysm was exposed and found to be firmly attached to the sternomastoid. This muscle was cut. The scalenus anticus was also cut. There was complete immobility of the right arm from pressure on the plexus. Part of the clavicle and sternum was resected. No vessel except the innominate could be ligated proximally. The aneurysm was inseparable from the carotid artery. The innominate artery was found after forty-five minutes and ligated 1 inch from the aorta with four strands of saddler's silk. The flaps were returned to position but could not be approximated. A compress was applied directly to the exposed tumor, and 10 per cent alcohol dressings were applied with pressure.

The postoperative course was uneventful until the twenty-first day, when the patient was up and feeling fine. That evening there was a sharp arterial spurt, and the patient lost 2 ounces (59.2 cc.) of blood. The ligature came away on the eighteenth day. From the twenty-ninth to the thirty-ninth day, the patient coughed and complained of pain in the chest. The tongue was red and the urine highly colored. The wound was healed except for an opening the size of a dime at the center. In the afternoon of the thirty-ninth day, there was another slight hemorrhage, which was easily controlled by a leather cushion apparatus. Several hemorrhages occurred on the fortieth day. On the forty-first day, the patient unbuckled the strap and bled to death almost instantly.

Autopsy showed that the stump of the innominate was left in a space as large as a hen's egg where the tissue had been carried away by the hemorrhage. The lungs were congested and showed fresh pleurisy. The aneurysm was clotted and hard and about one-fourth the original size.

CASE 20²¹ (surgeon, Smyth, 1864).—A mulatto, a man, aged 32, with an aneurysm of the right subclavian, was admitted to the hospital on May 9, 1864. Three months before the tumor had appeared. It was now the size of an orange with pulsation and bruit and lay in the posterior inferior triangle of the neck. The heart sounds were normal, and the pulses were equal. The patient had had considerable pain and numbness in the forearm and hand for two months.

On May 15, operation was performed, Mott's incision being used. There was no difficulty in placing a ligature $\frac{1}{4}$ inch (0.63 cm.) below the bifurcation. On tying this, all pulsation ceased. A ligature was tied about the carotid, 1 inch above its origin.

The temperature of the arm was increased immediately after operation. Two days after operation, the pulse was again felt in the wrist. Thirteen days after operation, the ligature came away. On the fourteenth day, there was a hemorrhage of 1 pint, which stopped of its own accord when the patient fainted. Slight hemorrhages

20. Cooper: Case of Ligating the Arteria Innominata, with Remarks, *Cincin. Lancet & Observer* 4:475, 1861.

21. Rogers: Case of Successful Ligation of the Innominata, *Am. Med. Times* 9:95, 1864; Successful Operation in a Case of Subclavian Aneurysm, *Biennial Retrospect New Sydenham Soc.* 32:346, 1865-1866, abstr. *Am. J. M. Sc.* 52:280, 1866. Smyth: A Case of Successful Ligation of the Innominate Artery, *New Orleans M. J.* 22:464, 1869. Thomson: Successful Ligation of the Innominata, Carotid, Vertebral and Internal Mammary Arteries, *Dublin J. M. Sc.* 62:481, 1876.

occurred the next two days, and on the sixteenth day the innominate ligature came away and the wound was filled with shot. No bleeding occurred for the next two weeks. The aneurysm became smaller and the pulsation became distinct at the wrist. On the thirty-third day, the shot was removed, and there was a severe hemorrhage. The shot was replaced. On the fifty-first day, there was a terrific hemorrhage, and the patient lost consciousness. On the fifty-fourth day, the right vertebral artery was ligated. The next day, all the shot was removed but no hemorrhage occurred. No pulsation was felt in the arm, which was cold and edematous. In a few days, this subsided. The ligature came away on the sixty-fourth day. Five years after, the patient was completely cured and had the use of his right arm. Sheen²² stated that "Aneurysm recurred ten years later. Internal mammary artery was tied October, 1874. In March, 1875, after opening an abscess above the clavicle, the aneurysm ruptured into this cavity, and he died April 6, 1875."

Autopsy showed that the innominate artery consisted of fibrous tissue beyond the ligature which was 1 inch from the origin of the artery. The carotid artery was occluded to its bifurcation, the subclavian almost to the thyroid axis and the vertebral to the fourth cervical vertebra.

CASE 21²³ (surgeon, Lynch, 1867).—A white man, aged 23, was admitted to the hospital on Dec. 19, 1866, with a pistol wound in the right side of the neck, 2 inches behind, and a little above, the angle of the jaw. The ball was said to have come out of the mouth. The wound was plugged. The face and neck were much swollen. There had been a profuse venous hemorrhage. Hemorrhages occurred about every fourth day, until Jan. 13, 1867. On that day the common carotid was ligated. On January 27, the ligature came away. From January 30 to February 2 the patient had chills, fever and cough. On the last day there was an alarming hemorrhage from the old wound, which was packed. On February 6, hemorrhage of 2 pounds of blood occurred. The patient was very much prostrated. On February 13, another alarming hemorrhage occurred, which was thought to be from the vertebral artery.

On February 13, the innominate artery was ligated in twenty minutes.

On the sixth day after operation the patient was restless. A hemorrhage of 1½ ounces (45 cc.) occurred from the original wound. There was considerable fever. On the twelfth day, there was a profuse hemorrhage, and the patient died.

Autopsy showed the ligature in the wound surrounded by a blood clot. The original pistol wound was deep and oval, extending into the neck 3½ inches behind and above the angle of the jaw. The posterior inferior triangle of the neck contained an abscess cavity filled with a blood clot into which the internal carotid and vertebral arteries opened. A partly organized clot filled the cardiac end of the innominate. There was an artery the size of a pigeon's quill arising from the innominate near the ligature. It was thought that this kept up the circulation on the cardiac side, so that when the ligature came away the clot was blown out with a fatal hemorrhage.

CASE 22²³ (surgeon, G. H. Porter, 1867).—A man, aged 43, was admitted to the hospital on June 11, 1867, with a pulsating tumor the size of a duck's egg of fourteen months' duration. Pressure had been applied for six weeks without benefit. On June 26, with the patient under chloroform, the axillary artery was compressed with a silver wire sufficiently to stop the pulse at the wrist. On June 28, the tumor was smaller and the wire was removed. On June 30, the tumor was

22. Lynch: Ligature of the Arteria Innominata, *Med. Gaz.* 1:100, 1868.

23. Porter, G. H.: Large Aneurysm of the Right Subclavian Artery Treated by Acupressure, *Dublin J. M. Sc.* 44:269, 1867.

firmer. Pressure was applied with a shot bag and ice. On July 17, the wound was healed. The aneurysm continued to enlarge, but was more solid. It was decided to use pressure on the innominate with an instrument somewhat like a lithotrite.

On July 31, with the patient under chloroform, an incision was made from the anterior edge of the sternomastoid 2 inches long to the sternum and then outward 2 inches along the right clavicle. The sternomastoid was cut. The sternohyoid and sternothyroid were cut. The carotid was traced down to the innominate, and the innominate was dissected out behind the sternum. The instrument was passed around the innominate, and the artery was obliterated by making the blades approach each other. The operation took forty minutes. The wound was closed about the instrument.

After the operation the patient had pain in the dorsal region and experienced difficulty in swallowing. Five hours after operation there was a slight pulsation in the tumor. Twenty-seven hours after, the pulsation returned; when the instrument was screwed tighter, it stopped. The patient still had difficulty in swallowing. After thirty-six hours, the pulsation returned; after 60 hours, the instrument was removed and pulsation returned. The tumor was firmer; the difficulty in swallowing stopped when the instrument was removed, and there was no hemorrhage. Nine days after operation, the wound was healing and the tumor seemed as previously. In the evening there was violent arterial hemorrhage, which was controlled by pressure. On the morning of the tenth day, a slight hemorrhage occurred. A violent hemorrhage occurred at night, with immediate death.

Autopsy showed slight atheroma of the aorta and an aperture in the innominate artery just below the bifurcation, which was sloughing at the edges. There was some fibrin in the tumor. The axillary artery was narrowed at the site of that operation.

CASE 23²¹ (surgeon, Bickersteth, 1868).—A man, aged 42, was admitted to the hospital on April 15, 1868, with an aneurysm of the subclavian artery the size of a hen's egg, due to a strain three weeks before.

On May 5, an incision was made along the anterior border of the sternomastoid muscle and out along the clavicle. The common carotid was exposed. This was followed down to the innominate, the sheath of which was opened. A thread was passed with a needle and then a lead wire. An instrument was passed down and the lead wire drawn tight, compressing the artery. This was left on forty-eight hours, when the pulsation returned in the aneurysm. The clamp no longer worked.

On May 7, the wound was reopened, and it was found that the sawing motion had cut the lead wire. Two strong silk ligatures were tied, one above and one below the wire.

A hemorrhage occurred the fifth day after operation, and on the sixth day, three hemorrhages. Loose shot was placed in the wound, but despite this the patient died rapidly at the last hemorrhage.

Autopsy showed a healthy wound. There was a clot firmly closing the innominate artery from its origin to the ligature. The carotid and the subclavian as far as the aneurysm were empty. The aneurysm and the subclavian beyond were clotted firmly. The hemorrhage was from the distal side of the ligature.

CASE 24²⁵ (surgeon, A. B. Mott, 1868).—The history of this case was not given. The innominate artery and carotid were ligated simultaneously. The liga-

24. Bickersteth: Case of Subclavian Aneurysm Treated by Temporary Compression of the Innominate Artery, Followed by Ligature, *Lancet* 2:815, 1872.

25. Wyeth: *Essays in Surgical Anatomy and Surgery*, 1879, p. 168.

ture was separated on the twentieth day after operation. There was no hemorrhage from the wound. On the twenty-third day, the patient died from hemorrhage into the pleural cavity when the sac ruptured.

CASE 25²⁶ (surgeon, Partridge, 1870).—A man, aged 32, was admitted to the hospital on April 17, 1870, with aneurysm of the right carotid artery of one and one-half years' duration. The common carotid was tied, on April 19, with the patient under chloroform anesthesia. The tumor decreased in size. On April 26, the right eye became congested and gangrenous. The ligatures separated on May 2. That evening the patient was feverish and coughed, and had a sudden arterial hemorrhage from the wound. The house surgeon stopped this by pressure of the vessel against the back of the sternoclavicular joint.

On May 2, one hour after the operation hemorrhage started. The original wound was enlarged, and the innominate artery was ligated just below the bifurcation. The patient died an hour and a half later from shock.

Autopsy showed suppuration. The cardiac end of the carotid at the ligature was open. The aneurysm was found to involve the entire extracranial internal carotid artery.

CASE 26²⁷ (surgeon, O'Grady, 1873).—A man, aged 60, had a subclavian and axillary aneurysm of three years' duration. The inner third of the clavicle was removed. The innominate artery was exposed and tied, and the common carotid was tied near its origin. Fifteen hours after operation, the respiration was changed markedly. Serous apoplexy occurred resulting in death.

Autopsy showed good closure of the vessels and effusion into the cerebral ventricles.

CASE 27²⁸ (surgeon, Buchanan, 1880).—A man, aged 40, was admitted to the hospital on April 19, 1880, with a pulsating tumor at the inner end of the right clavicle the size of an orange, of four months' duration. He complained of severe pain in the right arm. Medical treatment gave no relief. On May 14, galvano-puncture was done. There was oozing from the puncture hole for some time. The tumor became larger. On May 24, it measured 22 inches (55.5 cm.) in circumference. A sharp hemorrhage occurred on June 1.

On June 1, with the patient under chloroform, an incision was made along the carotid vessels and transversely across the tumor. There was a gush of arterial blood, which was controlled by hand pressure. The clots were turned out. An opening was found at the bifurcation. A finger passed behind the innominate stopped the hemorrhage. A ligature was applied. The wound was closed, but the patient died in a few minutes.

CASE 28²⁹ (surgeon, W. Thomson, 1882).—A man, aged 49, was admitted to the hospital on Feb. 7, 1882, with an aneurysm of the right subclavian artery of ten months' duration. There had been pain in the right arm for two and a half

26. Partridge, S. B.: Case of Aneurysm of the Right Internal Carotid; Ligature of the Common Carotid; Secondary Hemorrhage; Ligature of the Innominate; Death, *Indian Ann. M. Sc.* **14**:232, 1870-1871.

27. O'Grady: Ligature of the Innominate Artery at Mercer's Hospital, London, *Med. Press & Circ.* **15**:386, 1873. Sheen (footnote 9, p. 17); On Ligature of the Innominate Artery, *Ann. Surg.* **42**:17, 1905.

28. Buchanan: Aneurysm of Innominate Artery: Galvano Puncture; Rupture of Sac; Ligation of Innominate Artery, *Glasgow M. J.* **14**:152, 1880.

29. Thomson, W.: On a Case of Ligature of the Innominate Artery for Subclavian Aneurysm, *Brit. M. J.* **2**:722, 1882.

years. On admission, the tumor in the right side of the neck was pulsating violently; it measured $2\frac{1}{2}$ inches in diameter. The patient was treated medically, as he refused surgical treatment. He returned on May 22. The tumor measured $3\frac{3}{4}$ inches. Pulsation ceased at times, but never for long.

On June 8, an incision was made along the sternomastoid and clavicle. The sternomastoid was turned upward. The carotid was exposed. The bifurcation was very deep. A ligature of ox aorta was passed around the innominate artery. Pressure stopped the pulsation. The ligature was tied with three knots and moderate firmness. The wound was closed with drainage at the lower angle.

The arm was protected with wadding. Partial amnesia and coldness of the left side of the face were noted immediately after operation; the pupils were equal. The symptoms were gone by evening. The patient experienced considerable pain. Two days after operation, severe pain was felt in the shoulder; there was a slight serous discharge. On the fourth day, the wound was healed except at the drainage tube. This was cleaned and replaced. On the sixth day, the tube was replaced by catgut. On the eighth day, it was draining pus. On the fourteenth day, pain developed in the right eyeball and in the head; the temperature rose in the evening. On the seventeenth day, the ligature and part of the artery came away. On the twenty-eighth day, there was pulsation at the apex of the flap; a hemorrhage of 3 ounces occurred. A severe hemorrhage occurred on the thirty-seventh day, but ceased spontaneously; more pressure was applied. On the thirty-eighth day, there was no hemorrhage, and the patient was very weak. On the fortieth day, dyspnea and much pain developed. The patient died in the morning.

Autopsy of the wound showed that the aneurysm involved the second and third portions of the subclavian artery. There was an ulceration at the junction of the three vessels with some pus, and this led to a cavity behind the sternoclavicular joint which in turn communicated with the sinus. There were clots in all the big vessels. Some pus was found. The aneurysm had a laminated clot. The innominate was blocked with a clot, which apparently became infected from the ulceration; this was probably due to pressure of the drainage tube.

CASE 29³⁰ (surgeon, William Banks, 1883).—A man, aged 50, was admitted to the hospital on Feb. 10, 1883, with an aneurysm of the third portion of the subclavian artery.

Operation was performed on February 26, under asepsis. A silk ligature was passed about the innominate artery with some difficulty, as the bifurcation was low. This was used to apply kangaroo tendon ligatures which were tied to occlude and not crush, with three knots. Pulsation ceased in the aneurysm for two minutes. It then returned slightly, and the carotid was tied. Pulsation again ceased.

After the operation there was a slight return of the pulse during the evening. The patient was very restless the first few days. The wound healed by primary union. Pulsation returned with force on the third day, despite pressure from a shot bag. Sixty-seven days after the first operation, the subclavian artery was tied because the tumor was much worse. This was difficult owing to the size of the tumor. During the operation, the vein was opened, and air entered it. There was no bad result. The aneurysm ceased pulsating immediately. The wound was infected. The patient developed pneumonia, which cleared up, but death occurred from hemorrhage from the sinus thirty-seven days later.

30. Barwell: Case of Simultaneous Double Distal Ligature of the Carotid and Subclavian Arteries for High Innominate Aneurysm, *Brit. M. J.* 1:230, 1885.
Jacobson and Rowlands: *Operations of Surgery*, ed. 5, p. 805.

CASE 30³¹ (surgeon, Bull, 1884).—The patient had a subclavian aneurysm. The innominate, the right common carotid and the vertebral arteries were ligated simultaneously with double chromic catgut. The patient died on the thirty-third day from hemorrhage.

At autopsy the innominate was twice its normal size, thick and atheromatous. The carotid was firmly closed with a clot. The vertebral contained a loose clot, and the end of it was embedded in granulating tissue. The aneurysm was of the second and third portions of the subclavian. The aneurysm was the size of a duck's egg and contained bloody pus and clot.

CASE 31³² (surgeon, Annandale, 1885).—A man, aged 53, was admitted to the hospital on May 14, 1885, with a swelling in the right supraclavicular region of thirteen months' duration. He had been treated medically for one month. The mass was the size of an orange and pulsated. The heart sounds were faint over the aortic area. Pain was felt in the right side of the chest and shooting down the back.

On May 27, a median incision was made and the innominate artery was exposed and compressed with an instrument behind the sternoclavicular joint. All pulsation ceased. A rubber tube was passed down so that one extremity was behind the artery and the other protruded from the wound. The operation was done under asepsis.

On the second day after operation the temperature was 102 F.; there were pain and a slight cough. On the fourth day, the wound was dressed. It had almost healed except about the tube. On the eleventh day there was a small amount of blood on the dressings. On the twelfth day, a severe hemorrhage occurred, which was stopped by pressure with the finger on a hole in the innominate artery. The compressor was applied, as ligation was impossible. The hemorrhage stopped. The patient died five days later.

At autopsy an ulceration was found on the posterior surface of the innominate artery just below the bifurcation. This was the point where the pressure of the tube was applied.

CASE 32³³ (surgeon, Helferich, 1886).—The patient, a sailor, fell and injured his right shoulder four years previous to admission to the hospital. Some months later, he noticed a tumor below the right clavicle, which pulsated. It increased in size slowly for two years, and then rapidly. On admission, Jan. 22, 1886, there was a tumor twice the size of a child's head on the anterior wall of the chest below the clavicle. Sensory disturbances were noticed in the right hand. The tumor was almost rupturing.

On January 23, an incision 12 cm. long was made along the anterior margin of the right sternomastoid. The sternal portion of the sternomastoid was cut. The innominate was exposed, and the two heavy catgut sutures were tied. The pulsation in the tumor ceased. The aneurysm was emptied by compression, but it soon refilled. The common carotid was ligated. Still the aneurysm refilled. The subclavian was ligated in the third portion. The tumor still filled moderately. The wound was closed with two drains at the upper and lower margin.

31. Bryant: The Operative Treatment of Aneurysm of the First and Second Portions of the Subclavian, *Med. Rec.*, N. Y. **39**:305, 1891. Burrell: Ligature of the Innominate Artery with Report of a Case, *Boston M. & S. J.* **133**:125, 1895.

32. Annandale: On Compression of the Innominate Artery with Notes of a Case, *Lancet* **1**:481, 1886.

33. Ulrich: *Inaug. Dis.*, Greifswald, 1887, p. 14.

On the first day after operation, the patient was unconscious. There was edema of the larynx. The pulse rate and temperature were normal. Circulation in the right arm was sufficient. On the second day, the patient died.

Autopsy showed edema of the brain and anemia of the right side. The right vertebral artery was thrombosed. The probable cause of death was embolus of the brain, which was thought to result from repeated emptyings of the sac.

CASE 33²¹ (surgeon, May, 1886) —A man, aged 30, was admitted to the hospital on March 3, 1886, with a large aneurysm of the right subclavian of nine months' duration. He complained of numbness and shooting pains down the arm. There was a swelling measuring 3 by 2½ inches in the right side of the neck over which the common carotid could be felt. There was pressure on the brachial plexus, with pain, numbness and atrophy, mostly in the radial distribution. No edema was present. There was some clubbing of the fingers. The right pupil was smaller than the left. Medical treatment was given for about three and a half weeks.

Operation was performed on March 27, with the patient under chloroform. An incision was made along the inner third of the clavicle, meeting another over the common carotid. The sternomastoid, sternohyoid and sternothyroid were cut. The carotid sheath was opened, and the carotid artery was traced down to the innominate, which was found to be large. Pressure on this controlled the pulse in the carotid and in the aneurysm. A needle was passed with an aorta ligature after considerable difficulty from adhesions. This broke, and a cord of five or six medium catgut ligatures was used which was tied tight, but not tight enough to crush the artery. Three knots were used, and the ligature was cut. The wound was closed, and a tube and gauze drain inserted in one corner. The Lister spray was used. There was no pulse at the wrist or in the aneurysm.

A faint pulse was felt at the wrist four hours after operation. On the first day, pain and burning were felt in the arm. A small pulse was noted at the wrist and temple. On the second day, the wound was dressed, it was clean. The tube was removed. Pulsation had returned to the aneurysm with half the force that was noted before operation. On the ninth day, the aneurysm was smaller and harder. More pain was felt. On the fourteenth day, a small blood stain was seen on the dressing. On the fifteenth day, a sharp hemorrhage occurred, on the sixteenth day, several small hemorrhages occurred which were controlled by pressure, and on the seventeenth day, a severe hemorrhage. Death occurred on the eighteenth day.

At autopsy, the bottom of the sinus was found to be the artery. The knot could be felt in this position. There was a large aneurysm of the subclavian almost filling the thoracic aperture. All the branches of the artery opened into the sac. There was a small adherent clot and a large postmortem clot. The left carotid was small. The aorta and innominate arteries were atheromatous. There was a constriction of the vessel at the ligature. No pus was present. A small ulceration was seen under the knot. No coats were broken. The vessel was occluded except for ulceration.

CASE 34²² (surgeon, Durante, 1887) —A white man, aged 45, was admitted to the hospital with a pulsating tumor of the right supraclavicular region, the size of an apple. For two years there had been a tingling of the right thumb, a sense of heaviness in, and vague pains over, the entire arm. The aneurysm was of the second part of the subclavian artery.

34 May. Ligature of the Innominate Artery, *Lancet* 1:656 and 1064, 1886

35 Henderson. Ligature of the Innominate, *Lancet* 1:876, 1887. Spencer

Experiments in Ligature of the Innominate, *Brit M J* 2:73, 1889

Operation was performed on March 25, 1887, the incision of Mott being used. The innominate, carotid and vertebral arteries were ligated with no. 3 phenolized catgut; the innominate was ligated just below its bifurcation and again a little lower. The wound was closed with slight drainage at the inferior angle.

On the fourth day after operation, there was a slight serous drainage when the wound was dressed, and the tube was shortened. On the ninth day, the wound was united except at the sinus. The drain was removed. On the twelfth day, the temperature was 103 F. Pus exuded from the sinus, so the tube was replaced. On the thirteenth day, the temperature was 104 F. On the fourteenth day, there was right-sided hemiplegia, which disappeared in half an hour, except for paralysis of the right side of the face and of the tongue. Death occurred on the sixteenth day.

At autopsy the vessel was found closed and healed. There was an embolic softening of the left caudate nucleus of the brain.

CASE 35³⁶ (surgeon, Lewtas, 1889).—A youth, aged 20, was admitted to the hospital on May 13, 1889. He had been wounded above the right clavicle one month before. For the past three days, he had had slight hemorrhage with acute pain in the right side of the neck, and there was a swelling as large as a fetal head. There was thought to be a foreign body present. The wound was probed without result. A piece of gun breech was removed with the finger. This caused a smart hemorrhage which could be stopped only by putting the finger into the right subclavian artery. The patient went into coma from the hemorrhage.

On May 13, an incision was made along the lower end of the right sternomastoid muscle. A catgut ligature was passed around the carotid and used for traction. By means of this, a catgut ligature was passed down around the innominate just proximal to the bifurcation and tied. The operation was stopped, as the patient's condition was desperate.

After several hours, the wound was closed and dressed, and a drain was inserted into the original wound. Both wounds healed by primary union. The patient was discharged from the hospital forty-three days later. At that time, his right hand was in a sling. There was no right radial pulse, but feeble pulsation was felt in the right brachial artery.

CASE 36³⁷ (surgeon, Twynam, 1889).—A girl, aged 18, was thrown from her horse on July 21, 1889, fracturing her right clavicle. Five days later there was severe pain over the injury, with a swelling the size of a walnut. She was admitted to the hospital on August 19, with a diagnosis of aneurysm and fracture. She had great pain over the injury and down the inner side of the arm. The swelling measured 6 by 5 inches. Expansile pulsation was felt over the swelling.

On August 22, with the patient under chloroform, an incision was made by Spencer's method. The innominate artery was ligated $\frac{3}{4}$ inch below the bifurcation, after some difficulty in making it out. The carotid was ligated 1 inch above. The ligatures were cut short; the wound was closed without drainage. The pulse in the tumor ceased at once.

After operation, the tumor became harder. Pain became less and the arm remained warm. On the first day after operation, the patient became comatose; paralysis of the left side of the face and of the right side of the chest developed. Death occurred eighteen hours after operation.

36. Lewtas: Traumatic Subclavian Aneurysm: Ligature of the Innominate and Carotid Arteries: Recovery, Brit. M. J. 2: 312, 1889.
37. Twynam: Traumatic Subclavian Aneurysm: Ligature of the Innominate and Carotid Arteries; Death, Lancet 1:1352, 1890.

Autopsy showed the sac to be coagulated, communicating with the first part of the subclavian in the anterior wall. The inner coat of the innominate was ruptured. The ligature closed the artery. Autopsy was not performed on the brain, but probably there was a cerebral thrombosis.

CASE 37³¹ (surgeon, Jacobson, 1890).—A man, aged 48, had an aneurysm of one year's duration, 6 by 4 inches, in the axilla and subclavian space. He had chronic bronchitis and emphysema. In February, 1890, with the patient under chloroform, an incision was made along the right sternomastoid and the clavicle. The sternomastoid was cut. The inner third of the clavicle was resected. The innominate was found, and an ox aorta ligature was passed from without inward. The ligature was tied without injury to the coats, and pulsation ceased. The carotid was tied once, 1 inch above its origin. The wound was closed with a drainage tube.

After operation, pulsation ceased and never returned. On the third day, the aneurysm was much smaller. The patient was delirious. Death occurred on the tenth day. The wound was closed and clean.

At autopsy, pus was found about the ligatures. The vessel walls were soft. The aneurysm and vessels had clotted. There was valvular disease of the heart, and bronchopneumonia at the bases of both lungs. The brain was normal.

CASE 38³² (surgeon, Helferich, 1890).—A man, aged 39, was admitted to the hospital on March 11, 1890, with a pulsating tumor of both sides of the neck of eleven months' duration. He had intermittent pain in the shoulder and neck and about the tumor. The tumor measured 7 by 17 cm., and extended below the manubrium. The radial pulses were equal, and the temporal pulse was weak on the right. The right pupil was larger than the left. Diagnosis of innominate aneurysm was made.

On March 21, an attempt was made to ligate the innominate artery. With the patient under general anesthesia an incision was made parallel to and above the clavicle. The sternomastoid was dissected from the tumor. The tumor was adherent. An attempt was made at subperiosteal resection of the clavicle. As the clavicle came away, there was a flow of dark fluid. This was followed by sharp arterial hemorrhage, which was controlled by the finger. There was a cavity extending deep into the thorax toward the spine. The artery could not be found. The wound was packed with iodoform gauze to stop the hemorrhage, and it was closed with silk.

After operation, pulsation in the tumor was slightly less. Suppuration began on the fourth day. No hemorrhage occurred during the first week. The packing was removed on the seventh day. There was some redness and gangrene of the skin. On the eighth day, cough and bloody sputum were noted. On the ninth day there was a hemorrhage of 500 cc., and on the fifteenth day another hemorrhage of 250 cc., which was controlled by pressure. The patient was delirious, and died on the sixteenth day.

Autopsy showed an infected wound, pneumonia and dilatation of the innominate artery. A large sac just beyond was filled with a clot. The subclavian artery was enlarged, the carotid obliterated. The sac extended to the spine and to the left carotid. There was a sinus from the sac to the operative wound.

38. Jacobson and Rowlands (footnote 30, second reference).

39. Richter, J.: A Case of Aneurysm of the Innominate and Right Common Carotid, Dissertation, Greifswald, 1890.

CASE 39⁴⁰ (surgeon, Coppinger, 1893).—A man, aged 53, was admitted to the hospital on Dec. 5, 1892, with an aneurysm of the second and third parts of the subclavian artery as large as a hen's egg. The mass was tense, elastic and had a thrill. There was an axillary tumor the size of a walnut. The pulse at the wrist was weak. There was pain on the inner side of the forearm.

On Jan. 9, 1893, a vertical incision was made over the carotid and a transverse incision over the inner end of the clavicle. The anterior jugular vein was tied. A silk ligature was passed around the carotid, and the dissection was carried down to the innominate, which was ligated with silk from the outer side. The carotid was tied in two places and cut. The operation was aseptic and lasted thirty minutes.

On the fifth day after operation, the wound was dressed and was normal. On the twenty-seventh day, the patient was in good health. The temperature and pulse were normal for three weeks. The wound was practically closed. The right arm was normal. No pulse was felt in the radial or brachial arteries and no pain. On the forty-ninth day the condition was the same, except that the wound was healed. No hemorrhages occurred and no pulsation was felt in the aneurysm or in the brachial or radial arteries. The patient was seen on August 2, in good health, with a small hard swelling over the clavicle and no pulse at the right. The right arm was strong. Two and one-half years after operation, he was in good health.

CASE 40⁴¹ (surgeon, Hernandez, 1894).—On March 19, 1894, in Mexico, a youth, aged 18, received a knife wound low down in the region of the right carotid artery. He tried to stop the hemorrhage with two handkerchiefs, and rushed to a nearby physician. Two physicians were present, who removed the handkerchiefs, causing a sudden increase in the hemorrhage. A surgeon was called after pressure was reapplied. A few minutes later, the handkerchiefs were entirely soaked with blood. There was no temporal pulse, and the bleeding was apparently from the carotid.

With the patient under chloroform, an obtuse incision was used as advised by Farabeuf. The innominate artery was easily recognized, and in ten minutes a silk ligature was passed about it. The former wound was then opened, and there was profuse hemorrhage. The ligature was drawn tight, but the distal end still bled. This was caught with a clamp, which was left in place, as the patient was very weak. The lower part of the wound was sutured.

Four hours after operation, the patient was given a transfusion of 400 cc. of blood. A phlebitis developed the next day, but improvement was rapid. The clamp was removed in thirty-six hours. There was slight edema of the arm and loss of radial and temporal pulsation. The arm did not work as well as normal and was a little cold. There was right strabismus and ptosis but no cerebral anemia. The circulation was reestablished, as shown by a slight radial pulsation in about thirty-six hours. One month later, the patient was well. Two weeks after, he discharged a ligature from a small abscess at the inferior end of the scar. Six years after he showed a small pulsating tumor just behind the sternum, which has been present continuously.

40. Coppinger: Simultaneous Ligature of the Innominate and Carotid Arteries, *Med. Press & Circ.* **55**:153, 235 and 369, 1893; *Subclavian Aneurysm*, *Lancet* **2**:327, 1893; **2**:236, 1895; *New York M. J.* **57**:388, 1893; A Case of Successful Ligature of the Innominate Artery, *Tr. Roy. Acad. M., Ireland* **11**:243, 1893.

41. Hernandez, Albert: A Case of Ligature of the Innominate Followed by Cure: Thirteenth Congress International de Med., Sect. de Chir., 1900, p. 309; *abstr.*, *Wien. med. Bl.* **23**:559, 1900.

CASE 41⁴² (surgeon, Parham, 1894).—A white man, aged 48, ten weeks before admission to the hospital, while lifting, felt a severe pain in the right side of the neck, and a small lump appeared. The right internal and external carotid arteries had been ligated. The aneurysm continued to increase. On admission, Aug. 15, 1894, the pulse was almost imperceptible in the right radial and right temporal arteries. The right vocal cord was paralyzed. The right pupil was smaller than the left. The tumor was $7\frac{1}{2}$ inches (19 cm.) in circumference, and increased rapidly after admission.

On August 20, incision was made along the inner half of the right clavicle and down each side of the sternum. A $1\frac{1}{4}$ inch trephine was placed in the sternum. A small pulsating tumor was found just above the aorta. A large vessel was felt, which was probably the innominate. Ligation was impossible. The wound was packed. The patient died seventeen hours after operation, probably from shock.

At autopsy, the aorta was found to be dilated and rough. The innominate admitted the entire index finger. The aneurysm was of the bifurcation and included all three vessels.

CASE 42⁴³ (surgeon, Symonds, 1894).—A man, aged 53, was admitted to the hospital in October, 1894, with aneurysm of the second portion of the subclavian.

On November 5, an attempt was made to ligate the first portion of the subclavian artery through a vertical incision over the sternomastoid. As the needle passed, there was a sharp hemorrhage. This was repeated on a second attempt. A median vertical incision was made and joined to the other by a transverse incision. The sternal head of the sternomastoid was cut. The innominate and carotid arteries were tied with silk.

Two sinuses formed after operation. A piece of catgut and silk was discharged. Seven months after the aneurysm was hard. Function of the limb was returning. There was no radial pulse. The pulse was present in the carotid. In 1899, the patient was living and well.

Symonds stated in a letter on Oct. 1, 1904, that the "patient died some time ago of a general malady."

CASE 43⁴⁴ (surgeon, H. L. Burrell, 1895).—A white man, aged 54, two years before admission noticed difficulty in breathing. Six months later, he noticed a lump in the left side of the throat, which throbbed and choked him. The lump increased in size slightly. Examination on admission showed the heart enlarged with systolic and diastolic murmurs over the entire precordia. The liver was enlarged. The pulse was full in both wrists.

On July 15, 1895, an incision was made along the anterior edge of the sternomastoid muscle and outward 4 inches to the middle of the clavicle. The sternomastoid was cut at the sternal insertion. A fusiform aneurysm of the right subclavian, right carotid and innominate arteries was exposed. The upper half of the sternum and sternoclavicular joint was removed with bone forceps. The wound was kept wet because of air bubbling in the tissues, apparently from an opening in the pleura. The innominate artery was isolated and found to be $1\frac{1}{4}$ inches in diameter. A flat spatula was passed under the vessel, and a flat braided silk

42. Parham: Preliminary Report of a Case of Immense Cervical Aneurysm Involving the Innominate Bifurcation: Unsuccessful Attempt to Pass a Proximal Ligature; Death; Autopsy, New Orleans M. J. **23**:703, 1895.

43. Symonds: Lancet, Tr. Clin. Soc. **1**:1493, 1899. Jacobson and Rowlands (footnote 38). Sheen (footnote 9).

44. Burrell, H. L.: Ligature of the Innominate Artery with Report of a Case, Tr. Am. Surg. Assn. Phila. **13**:291, 1895; footnote 31, second reference.

ligature was passed with an aneurysm needle and tied with the square knot. This was gradually tightened until the coats gave way. A second ligature of silk was placed in the same way $\frac{1}{2}$ inch distal to the first, and was not tied quite as tight as before. The intention was to cut the artery, but this procedure seemed too dangerous. The wound was closed tight. Operation lasted one hour and fifteen minutes.

After operation, pulsation had disappeared from the neck and from the right carotid and the radial arteries. Cotton was packed around the arm. The right pupil was larger than the left; the right ear drum was anemic. There was no pain. On the second day, there was capillary circulation in the nails. On the fifth day, the fingers were pink and could move. On the sixth day, the wound was dressed. There was violent pulsation over the sternum. There was a small radial pulse. Some sutures were removed. On the seventh day, the numbness and prickling disappeared. On the tenth day, the wound was healed and all stitches removed. On the fifty-third day, there was slight swelling of the right arm, which lasted from three to four days. During this time, the patient was up and around. He left the hospital on the seventy-third day. He returned on the hundredth day with edema of the arm, and died suddenly on the hundred and fourth day.

Autopsy revealed hypertrophy and dilatation of the heart and of the aorta, with atheromatous patches. The right subclavian artery was dilated. The innominate artery was completely closed at the origin of the subclavian and carotid arteries. It was dilated proximally to this point. A ligature was found embedded in the walls of the artery. The lower ligature had severed the artery, but healed. Syphilis was made out on microscopic examination. Collateral circulation was found to be through the right carotid and the vertebral of the subclavian.

CASE 44⁴⁵ (surgeon, R. H. Harte, 1896).—A colored man, aged 26, was admitted to the hospital on May 31, 1896, with a pistol wound of the neck. The bullet entered the neck on the left side. The left arm was paralyzed. The forearm and hand were normal. There was dysphagia. A roentgenogram taken on June 1 showed the bullet on the right side of the neck anterior to the seventh cervical vertebra.

Operation was performed on June 1, with the patient under ether. An incision was made in the right side of the neck behind the posterior margin of the sternomastoid. The bullet was found in a pocket of pus close to the esophagus, behind the common carotid artery just above its origin. On June 4 a fistula developed, which soon healed. On June 12 there was a sudden hemorrhage, which was controlled by packing. On June 14 there was another sudden hemorrhage, which was controlled by placing a finger in the depth of the wound. On July 16 an incision was made in the line of the carotid vessels, exposing the common carotid. A ligature was placed around them, but this did not stop the bleeding. The sternal end of the clavicle was dislocated; an abscess cavity was found at the bottom of the wound. Another ligature passed just above the origin of the carotid entirely controlled all bleeding. On July 26 there was a second hemorrhage. The patient was in a poor condition, but bleeding was controlled by a finger.

On July 26, the old wound was opened. The proximal end of the carotid was found to be open; the clavicle was turned outward. The innominate artery was found and ligated with silk a short distance proximal to its bifurcation. The right subclavian and the carotid arteries were also tied. The right internal jugular was ulcerated, so that it ruptured and was tied with a double ligature. The edges

45. Harte, R. H.: Ligation of the Innominate Artery for Hemorrhage with Report of a Case, *Ann. Surg.* 26:489, 1897.

were approximated with silkworm gut. The patient was given an infusion, but died in a few hours.

Autopsy showed that the esophagus was ulcerated, and had a fourth of an inch opening. There was an abscess of the brain in the right temporosphenoidal lobe.

CASE 45¹⁰ (surgeon, G. W. Gay, 1896).—A white woman, aged 39, had noticed dyspnea and dysphagia and painful pulsation at the root of the neck for two years. There was a dull, aching pain in the back of the right axilla. During the six months before admission to the hospital all the symptoms had grown worse. On admission, Oct. 19, 1896, there was a tumor $1\frac{1}{2}$ inches in diameter in the right side of the neck.

Operation was performed on October 27, with the patient under ether, and sitting in a chair. An incision was made from the left sternomastoid down to the sternum and out along the right clavicle. The sternomastoid muscle was divided. The sternoclavicular joint and the upper portion of the sternum were removed. The innominate was exposed, and the sheath was opened. The artery was found to be 2 inches long and 1 inch in diameter. Three ligatures of braided silk were used, the first one $\frac{3}{4}$ inch from aorta, the second $\frac{1}{2}$ inch distal to this and the third one in the same place. All the ligatures were passed from within out, tied with square knots and cut through. The wound was closed in layers with silk, and a small silk drain was placed at the angle. The arm was wrapped in absorbent cotton. The operation lasted one and one-half hours.

After operation, pulsation in the tumor and radial arteries ceased at once. Seven hours later, there was slight pulsation in the right radial artery. On the fourth day, the wound was dressed and was found to be normal. On the sixth day, the temperature was 100.4 F. There was infection of the wound; the flap was red and swollen, but the patient's general condition was much better than before operation. On the tenth day, the wound was healed except for a small sinus at the angle $1\frac{1}{2}$ inches long. On the twenty-third day, the sinus closed. On the thirty-second day, while the sinus was being washed out, a slow welling up of blood occurred which was easily controlled by pressure. Ether was given. The incision was opened. A small cavity was found with a sinus extending toward the deep ligatures. The right carotid was exposed and tied with silk 1 inch from its origin, and the wound was closed. The sinus was packed with iodoform gauze. On the thirty-fourth day, the temperature was 104.5 F. A brisk hemorrhage occurred. On the thirty-fifth day, there was a hemorrhage. On the thirty-sixth day, the sutures were removed. The temperature was normal. On the thirty-eighth day, the patient had some difficulty in moving the right arm. It felt numb and cold. On the thirty-ninth day, a profuse hemorrhage occurred. On the forty-first day, the temperature was 105 F. at night. There was a severe hemorrhage, and the patient died.

Autopsy showed a cavity about the innominate artery the size of a walnut communicating with the sinus and filled with clot and serum. Two ligatures were found together about the innominate in this cavity. The single ligature proximal to this and the artery were lost. The carotid was closed by a ligature. The subclavian artery and branches were much dilated. A diagnosis was made of rupture of the innominate artery proximal to the ligatures. Myocarditis, arteriosclerosis and multiple abscess of the kidney were found. *Staphylococcus aureus* was cultivated from the heart, liver, spleen and kidney. Microscopic examination

46. Gay, G. W.: A Case of Ligature of the Innominate Artery for Aneurysm, Boston M. & S. J. 137:73, 1897.

of the arterial wall showed it to be necrotic, with staphylococci present. It was found on investigation that a new sterilizer had been used for ligatures, which was later found to be faulty.

CASE 46⁴⁷ (surgeon, Schumpert, 1898).—A negress, aged 42, was admitted to the hospital with a pulsating tumor the size of a large marble behind the inner third of the right clavicle. She suffered from dyspnea and a dull aching pain in the tumor. A diagnosis was made of aneurysm of the common carotid near its origin.

An incision $7\frac{1}{4}$ inches long was made at the anterior border of the sternomastoid down across the sternum. The sternal portion of the sternomastoid was cut. The anterior jugular was ligated. The carotid artery was exposed, and traced. The aneurysm was found to be of the bifurcation. The innominate artery was traced down to the aorta and ligated $\frac{1}{4}$ inch from the aorta with no. 8 braided silk passed from within out and tight enough for occlusion without severing.

After operation, the wound healed by primary union. There was a difference in temperature in the two arms during the first two days. The pulse rate was 40 for the first forty-eight hours, then 68. No pulse was felt in the arm or temple. On the fifth day, the patient was in coma and she died on the following day.

Autopsy showed some softening and slight atrophy of the right side of the brain. The ligature was encysted without inflammation.

CASE 47⁴⁸ (surgeon, B. G. A. Moynihan, 1898).—A white man, aged 31, noticed a pulsating tumor on the right side of the root of the neck fifteen months before admission to the hospital. This gradually increased in size. There was a history of syphilis. The left radial and brachial pulse was absent. On admission, there was a large mass the size of a hen's egg, with expansile pulsation. The heart was normal. The right pulse suddenly stopped twenty-three days after admission. It returned later, but the tingling and aching in the arm continued. On Dec. 8, 1897, through an incision with resection of the clavicle, the aneurysm was resected between ligatures of the second portion of the subclavian and axillary arteries. On December 13, there were infection and erysipelas and a temperature of 104 F. On December 20, there was considerable drainage of pus. On December 25, the condition was the same. On Jan. 9, 1898, the gland in the axilla was incised, and antistreptococcus serum was given. There was a sudden hemorrhage from the flap which was controlled by pressure. On February 8, there was another hemorrhage. The wound was opened, and the subclavian was found to be bleeding very deep.

On this same day curved incision was made about the sternoclavicular joint, concave, upward and outward. The upper fourth of the sternum and the inner third of the clavicle were resected after holes had been bored. The innominate artery was reached immediately and the ligatures placed. The innominate and carotid were ligated and the hemorrhage stopped, but the patient died from shock one hour after operation.

Autopsy revealed a second aneurysm of the subclavian distal to the vertebral, which had ruptured.

47. Schumpert: Ligature of the Left Subclavian: Ligature of the Innominate Artery for Innominate Aneurysm, Also First Portion of Left Subclavian, *Med. Rec.* 54:337, 1898.

48. Moynihan, B. G. A.: A Case of Subclavian Aneurysm Treated by Excision of the Sac, *Ann. Surg.* 28:1, 1898.

CASE 48⁴⁹ (surgeon, A. L. Bennett, 1898).—A native in French Congo, aged 55, while on a walking trip in May, 1899, developed marked dyspnea and swelling in the right side of the neck, which had been progressing for many years. The right pupil was greater than the left. The trachea moved with the swelling, but there was no large tug.

Operation was performed on May 12, 1898. The anesthesia was administered, with the aid of native assistants, and the patient prepared for operation with soap, water and alcohol. An incision 10 cm. long was made along the sternomastoid and 11 cm. parallel to the clavicle. The sternomastoid muscle was cut. A large aneurysm of the carotid and first part of the subclavian was exposed. Part of the sternum and clavicle was cut away with much difficulty. Two flat tape ligatures, 3 cm. wide, were passed around the innominate artery with an aneurysm needle. One was tied 1 inch from the aorta, the other some distance distally, and the innominate artery was cut between the ligatures, leaving a 5 mm. stump on the proximal side. The operation was dry. All pulsation ceased at once in the neck, and there was no pulse at the wrist.

After the operation the patient did well until the third night, when he died suddenly from secondary hemorrhage. No autopsy was obtained.

CASE 49⁵⁰ (surgeon, B. F. Curtis, 1899).—A white man, aged 55, was admitted to the hospital with intense pain in the right arm of some months' duration. The heart was hypertrophied. There was generalized arteriosclerosis, especially of the right subclavian and axillary. Under the right clavicle there was a swelling 2 inches in diameter with expansile pulsation.

Operation was performed on Dec. 2, 1899. The sternum was split and divided transversely just above the second rib. The carotid and the subclavian were found, and then these were traced down to the innominate, which was isolated. A double heavy chromic catgut ligature was applied and tied simultaneously $\frac{3}{4}$ inch proximal to the bifurcation, but not with a stay knot. The artery walls were folded in easily. The ligature was tight enough to stop the pulsation, but not tight enough to injure the coats. Another single ligature was placed obliquely, distal to the double ligature. The bone was united with heavy wire. The wound was closed without drainage, except the lower angle between the skin and sternum.

For two days after operation there was considerable pain. The temperature varied from 102 to 104 F. The pulse rate was slow. No cerebral disturbance was noted. Four days after operation, there was a slight pulsation in the aneurysm and in the right radial artery. Four weeks after, when the patient got up, the pulsation increased. There was also pulsation in the carotid. Six weeks after operation, a small abscess at the upper angle of the scar was opened. On March 13, 1900, the common carotid and first portion of the subclavian were ligated distally to the superior thyroid branch. The pulse stopped in the aneurysm but not in the subclavian artery. The clavicle was wired, and the wound was closed. The temperature rose to 102 F. The inferior upper angle suppurated. There was some osteomyelitis. The wire was removed and fibrous union occurred. On October 29, the patient was in good condition with a strong union of his clavicle and no aneurysm.

49. Bennett, A. L.: Ligature of the Innominate for Aneurysm of the Right Common Carotid and Subclavian, *Colorado M. J.* 6:467, 1900.

50. Curtis, B. F.: Ligature of Innominate Artery, *Ann. Surg.* 31:626, 1900; Milton's Method of Exposing the Anterior Mediastinum Modified for Ligature of Innominate Artery, *ibid.* 34:472, 1901.

CASE 50⁵¹ (surgeon, DeLaup, 1900).—A negro, aged 58, was admitted to the hospital on June 2, 1900, with a pulsating tumor the size of an orange in the right side of the chest of six months' duration. Constant pain was felt in the right shoulder for several weeks. There was general arteriosclerosis. The heart was enlarged, a double murmur being heard. After two weeks of medical treatment, he showed no improvement.

On June 16, with the patient under chloroform, an incision 3 inches long was made from the trapezius to the sternomastoid. The aneurysm was found to be of the second and third portions of the subclavian. The incision was prolonged to the manubrium, and the sternomastoid, sternohyoid and sternothyroid were cut. The inner part of the clavicle and part of the manubrium were resected. A fusiform aneurysm of the bifurcation of the three vessels was found. The innominate artery was twice the normal size at its origin. A kangaroo ligature was tied 1 inch from the aorta with three square knots without rupturing the coats. A kangaroo tendon ligature was tied distally, probably rupturing half way to the aorta. A braided silk was tied completely obliterating the radial pulse. All ligatures passed from within out. The operation lasted two hours. There was some shock, and therefore the wound was closed without ligation of the carotid.

After operation pulsation was absent in the aneurysm and subclavian artery. The arm was wrapped. A slight pulse was felt in the right radial artery at the end of four hours. On the first day, the patient had headache and was restless and mentally dull. On the third day, the tumor was denser and smaller; the dressing was stained. On the sixth day, pus was present at two sutures. On the eighth day, there was a sinus $1\frac{1}{2}$ inches deep. On the tenth day, delirium became worse. On the eighteenth day, slight hemorrhage occurred. For fear of further hemorrhage the carotid and vertebral arteries were tied with silk, with the patient under chloroform anesthesia. He died as the wound was closed. Autopsy showed a hypertrophied heart and valvular disease. The innominate was surrounded by a thick ring of tissue. The silk ligature was in the lumen. The kangaroo ligature was absorbed. The sinus did not communicate with the lumen. Circulation was apparently reestablished. The carotid and subclavian arteries and their branches were dilated. The aneurysm of the third subclavian and axillary was clotted.

CASE 51⁵² (surgeon, von Ruediger, 1901).—A woman, aged 37, had noticed a swelling in the right shoulder and neck for five years. The right arm became weaker, and for one year there was severe headache, hoarseness and dyspnea. There was a pulsating tumor the size of a hen's egg under the right sternomastoid. The growth extended under the clavicle and sternum. The temporal pulse was weak on the right, and the right radial pulse was lacking. The right arm was weaker than the left. There was vocal paralysis on the right side. A diagnosis of innominate aneurysm was made.

On March 19, 1901, a curved incision was made, concave upward and outward. Part of the sternum and clavicle was resected. An enormous aneurysm extending into the thoracic cavity was exposed. The three great vessels lay on the anterior surface. The subclavian artery was finally discovered to communicate with the aneurysm. The subclavian was ligated distal to the opening.

51. DeLaup: A Case of Ligature of the Innominate Artery for Aneurysm, *Phila. M. J.* 7:171, 1901.
52. Von Ruediger: A New Method of Ligation of the Innominate Artery, *Wien. klin. Wchnschr.* 19:1514, 1906.

The innominate artery was ligated because of the difficulty of ligating the first portion of the subclavian. Pulsation stopped at once. The aneurysm was opened and bled severely. The sac was partially extirpated. The wound was packed and closed around the drains. The operation lasted two hours and fifteen minutes. The patient died of shock despite hypodermoclyses.

At autopsy the pathologic process described at operation was found. The aneurysm extended down into the thorax on to the right lung and was adherent to the pleura. There was edema of the lungs.

CASE 52⁵³ (surgeon, C. A. Ballance, 1902).—A man, aged 35, was admitted to the hospital on March 27, 1902. In the right root of the neck, there was a slight swelling 9 cm. long with expansile pulsation. The swelling extended under the manubrium. The right radial and carotid pulses were smaller than the left. The right pupil was smaller than the left and the right vocal cord was partially paralyzed. There was pressure on the right lung. The heart and aorta were normal. There was pain in the tumor, and the patient had a hacking cough. Medical treatment was given without effect.

On April 15, with the patient under chloroform, a median incision was made from the thyroid cartilage to the manubrium. The sternohyoid and sternothyroid muscles were separated. A finger was passed down beside the trachea to the arch of the aorta. The innominate was normal for the first half inch. The manubrium was incised vertically to the upper border of the second costal cartilage, cut across at this point and pulled apart. One-half inch of bone was removed from each side. The vessel was cleared, and a needle with four strands of gold-beater's skin (ox peritoneum) no. 4 was passed. This was tied with a stay knot, occluding without injuring the coats. The pulsation in the aneurysm ceased at once; the common carotid, which was distended but not pulsating, was tied with two strands of the same. This was needless, due to a clot. The wound was closed.

After operation there was no pulse in the right radial artery, and the right side of the face was colder than the left. Breathing was labored on the morning after operation. There was a left hemiplegia that night, and the patient died.

At autopsy the common carotid, internal carotid and middle cerebral arteries were thrombosed. No other disease was found. There was an aneurysm of the carotid, subclavian and innominate arteries.

CASE 53⁵⁴ (surgeon, Persons, 1904).—The patient was in the Naval Hospital at Norfolk, Va., for two weeks with repeated hemorrhages from a laceration of the right axillary artery. The bleeding point could not be located. Operation was performed, but after an ineffectual attempt to find the subclavian artery, owing to a clot, the innominate was ligated at the bifurcation. The patient died.

CASE 54⁵⁵ (surgeon, Sheen, 1904).—A white man, aged 46, had an aneurysm of the second and third parts of the subclavian artery of six months' duration. There was a pulsating swelling above the middle of the clavicle, 6 by 5 cm., extending from the sternomastoid to the trapezius muscle. The right radial, brachial and axillary pulse were just perceptible. The temporal and the carotid pulse were equal on the two sides. The fingers were bluish white.

53. Ballance, C. A.: Aneurysm Involving Innominate, Subclavian and Carotid Arteries, Treated by Proximal Ligation, *Lancet* 2:1180, 1902; Ligation of the Innominate Artery Innominate Aneurysm, *Brit. J. Surg.* 9:438, 1921.

54. Persons: Ligation of the Right Innominate Artery, *Rep. Surg.-Gen. Navy*, 1904, p. 272.

55. Sheen: A Case of Ligation of the Innominate Artery, *Brit. M. J.* 2:870, 1905; footnote 9.

On March 31, 1904, with great attention to asepsis and with the patient under chloroform, a median incision, 5 inches long, was made from the cricoid cartilage to the sternal notch. The carotid vessels were exposed and traced down. In dissecting the first part of the subclavian, the pleura was opened. This was packed with gauze. The innominate was exposed; two ligatures of stout floss silk were passed from without inward and tied with a Ballance and Edmunds' stay knot to occlude completely without injuring the coats. When the ligature was tightened, the temporal pulse disappeared. The carotid was tied with one suture in a surgical knot. The wound was closed tight.

Mental disturbance was noted for two days after operation. One day after, there was a slight return of pulsation. This increased for four days and was gone on the eighth. It increased later, but never was as strong as before operation. The pain continued. There was primary union of the wound. There was slight recurrent paralysis on the right side. The right radial pulse returned on May 17. On May 19, an attempt was made to ligate $\frac{1}{2}$ inch proximal to the sac; this was not successful, owing to bleeding. On June 2, the aneurysm and first part of the subclavian were exposed. A stout twist was passed around the latter and tied with a surgical knot. The pulsation ceased. The second suture was passed distal to the first. There was primary union. Circulation was not as good after this operation. Three weeks after this, there was no return of pulsation. Pain and tingling were much less. The radial pulse returned two months after operation. On December 16, the sac was flat, and had no pulsation. There was a slight pulse in the right radial and temporal arteries. None was felt in the right carotid and brachial arteries. The enlargement of the veins had disappeared. The pain was slight. The patient's condition was good.

CASE 55⁵⁶ (surgeon, Saigo, 1094).—A soldier, aged 22, was shot in the right side of the neck on Oct. 14, 1904. The shot went through the neck from the anterior border of the right sternomastoid to 2 cm. from the spine of the first dorsal vertebra. An aneurysm developed, with pain, difficulty in swallowing and ptosis on the right side. Pain was felt also in the arm down to the little finger. The tumor increased in size, the skin became tense and bluish and right-sided headache developed.

On November 23, with the patient under chloroform, a T-shaped incision was made over the clavicle and manubrium. The sternal end of the sternomastoid was cut. Part of the clavicle and part of the manubrium were resected. The innominate artery was isolated and ligated. The aneurysm was of the right carotid. The wound was closed with drainage.

On the first day after operation, there was pain in the wound; the pain in the arm and head was gone. No radial pulse was felt. There were slight emphysema and difficulty in swallowing. On the second day, the drain was removed. The tumor was smaller, and there was a large amount of grayish discharge. On the sixth day, the wound was reopened. There was a moderate amount of pus. The emphysema disappeared. On the tenth day, the tumor began to pulsate again. On the fifteenth day, the skin broke down and discharged tarry fluid. Healing was uneventful from that time. In August, 1905, ligation was done above and below the aneurysm, and the sac was resected. The patient made a good recovery.

CASE 56⁵⁶ (surgeon, Saigo, 1905).—A soldier, aged 24, was shot just above the right clavicle on March 5, 1905. He developed a varicose aneurysm of the right

56. Saigo: Traumatic Aneurysm in the Russo-Japanese War, *Deutsche Ztschr. f. Chir.* 85:577, 1906.

subclavian artery and vein. The wound healed in fifteen days. Severe pain was present over the tumor.

On April 6, 1905, with the patient under chloroform, an incision was made along the right clavicle with resection of its inner third. The innominate artery was doubly ligated and cut.

After operation the patient complained of cold in the right temple and cheek. The tumor recurred after thirteen days. The right pulse was weaker than the left. The right arm was emaciated. On August 4, an operation was again performed in the original scar. The new bone was resected. The subclavian artery was exposed. The aneurysm was excised after ligation of the subclavian artery and vein, proximally and distally. The pain was better after this operation. The patient was discharged on November 2.

CASE 57⁵⁷ (surgeon, W. S. Halsted, 1905).—A white woman, aged 50, was admitted to the hospital on Oct. 17, 1905, with aneurysm of the right subclavian artery of six years' duration. The aneurysm was wired in December, 1904. The heart was normal. There was a tingling in the fingers, but no paralysis of the nerves. The radial pulse was a little delayed. The tumor measured 7 by 8 cm.

On Nov. 17, 1905, two thirds of the clavicle and part of the first rib were resected. The innominate artery was partially ligated with a no. 33 aluminum band 1.5 cm. wide, wrapped twice around the artery and held in place by a heavy black silk ligature.

After operation the pulsation was reduced somewhat by the application of the band; the size was unchanged. On January 12, the blood pressure of the right arm was 100 and of the left arm 102. The subclavian artery was ligated. Pulsation in the aneurysm persisted after ligation on both sides of the aneurysm. There was no pulse in the tumor at the first dressing after the second operation. The patient was well on February 10. She was readmitted to the hospital on March 31, 1921. The aneurysm had disappeared. Function of the arm was not impaired. There was dilatation of the common carotid distal to the band.

CASE 58⁵⁸ (surgeon, Cuneo, 1905).—A woman, aged 49, was admitted to the hospital on Dec. 12, 1905, with an aneurysm of the aortic arch. She had had increasing dyspnea for six years, and the medical treatment had not improved her. She was hoarse, had severe dyspnea, was weak and emaciated and had severe pain.

On December 13, with the patient under chloroform, a right angle incision was made, and the sternomastoid was cut. The inferior thyroid veins were cut and tied. The innominate artery was tied at the middle with no. 2 silk, and the respirations ceased momentarily. The innominate artery was dilated proximally, being involved in the aortic aneurysm. The wound was closed without drainage.

After operation the radial pulse stopped but returned the next day, with no change in the pupil. The temporal pulse was present throughout. The first day after operation, the dyspnea was better and the tumor was small. The patient was discharged at the end of one week. She was in the hospital again from Jan. 12, to March, 1906, with bronchopneumonia. In December, 1910, she was living, and was much better than before the operation. The dyspnea was not so severe. There was no cough. The tumor was present, but was much harder.

57. Reid: Aneurysms in the Johns Hopkins Hospital, *Arch. Surg.* **12**:1 (Jan.) 1926.

58. Guinard: Ligation of the Innominate Artery for Aortic Aneurysm, *Bull. et mém. Soc. de chir.* **37**:800, 1911.

CASE 59⁵⁹ (surgeon, Curtis, 1907).—A white man, aged 59, was admitted to the hospital on Jan. 4, 1907, with aneurysm of the right subclavian artery.

Operation was performed on January 11. The manubrium was split to a point below the second rib and forcibly separated $1\frac{1}{2}$ inches. The innominate artery was exposed and ligated with no. 4 chromic catgut. Two ligatures were laid side by side and tied separately 1 inch above the origin of the artery. Another double ligature of the same was tied $\frac{1}{2}$ inch distal to the first, and the two threads were tied together. The bone was sutured with chromic catgut. There was no drainage.

All pulsation ceased in the arm, carotid and aneurysm immediately after operation. The pulse in the external carotid returned in two hours. The patient developed bronchopneumonia, and died four days after operation.

Autopsy showed an uninfected wound. Both ligatures were present, but the proximal was driven forward to the distal by pulsation. The internal coats were not ruptured. The vessel was folded together and closed. A clot filled the distal innominate, the subclavian and the aneurysm. The origin of the common carotid was also filled, but the artery was patent at its bifurcation. There was no clot in the innominate, proximal to the ligatures. The lungs showed purulent bronchitis and bronchopneumonia.

CASE 60⁶⁰ (surgeon, W. S. Halsted, 1907).—A colored man, aged 51, married, had an aneurysm of the innominate artery of one month's duration. The tumor increased from a small lump to the size of a baseball in one month. There was numbness in the right hand. The right pupil was smaller than the left. The symptoms began with a cough; then there was pain in the neck, ear and chest. The heart was possibly enlarged. The tumor measured vertically 8 by 11 cm. The right radial pulse was more compressible than the left.

On February 2, the innominate artery was ligated for an aneurysm involving the subclavian artery. Three heavy, braided white silk ligatures were tied close together, the most distal one completely occluding the artery. There was a small iodoform pack placed to a point of rupture in the pleura.

The pulse was felt at the wrist and in the temporal artery at 5 p. m. on the day of operation. There were no sensory disturbances. The next day the blood pressure in the right arm was 65, and in the left 124. Some edema of the arm was noted, but this subsided markedly. The grip was slightly weaker. The aneurysm continued to pulsate with two thirds of the former force. It became smaller, measuring 7 by 7 cm. On February 20, partial ligation of the right common carotid artery was performed and an aluminum band 8 mm. wide was placed above an aneurysm involving the subclavian, common carotid and innominate arteries. The band almost occluded the artery just below the bifurcation. That afternoon, at 3 p. m., the blood pressure in the right arm was 100, and in the left 145; at 8 p. m. it was 85 in the right arm and 145 in the left. After the second operation, the aneurysm was unimproved. It increased in size. The grip in the hand became weaker. The patient was discharged on June 11. He died on Jan. 1, 1908, of pneumonia. Autopsy was refused. The wife said that the aneurysm stopped pulsating and became hard before death.

CASE 61⁶¹ (surgeon, W. B. Burns, 1907).—A colored man, aged 27, was admitted to the hospital on Aug. 6, 1907, with swelling above the right clavicle

59. Curtis: Ligation of the Innominate Artery, *Ann. Surg.* 45:966, 1907.
60. Burns, W. B.: Successful Ligation of the Innominate Artery, *J. A. M. A.* 51:1671 (Nov. 14) 1908.

of one year's duration. Pain had been felt in the shoulder and down the arm for five months. The arm and hand were edematous and numb.

Operation was performed on August 9, with the patient under ether, Mott's incision being used. One ligature, with the largest size of braided silk, was tied around the innominate artery 1 inch from the bifurcation in a granny knot. The ligature was tight enough to approximate the vessel walls, but not to crush them. The operation lasted one hour and twenty minutes. Pulsation ceased at once.

On the second day after the operation, the edema, pain and numbness were gone. On the fourth day, there was suppuration of the wound. On the fifth day, counter openings were made, and wicks were inserted. The temperature fell and remained normal until the fourteenth day. On the fourteenth day, there was a hemorrhage which was controlled by packing and tight dressing. On the sixteenth day, a small hemorrhage occurred, the temperature rising to around 101 F. On the eighteenth day, there was another small hemorrhage. On the twenty-first day, the ligature was removed from the wound.

CASE 62⁶¹ (surgeon, Myles, 1908).—A man, aged 29, had a subclavian aneurysm. A median incision was made low in the neck, and the innominate artery was ligated. The right common carotid was doubly ligated and divided. The wound healed by primary union. Pulsation continued in the aneurysm, and ten days after operation there was a large subcutaneous hemorrhage. The wound was opened, and the stumps of the vessels were clamped and tied. Suppuration followed this operation, and the patient died at the end of one month.

Autopsy showed that the ligatures had slipped from the carotid artery.

CASE 63⁶² (surgeon, Herzen, 1908).—A policeman, aged 30, was shot in the right side of the neck, in the right arm and the right leg seven months before admission to the hospital. On the way to the hospital, he broke the right clavicle. The wound bled severely, and he was unconscious for three days. Three months later, a slowly increasing aneurysm appeared, with swelling of the right cheek and arm. On his second admission, he showed scars of the right leg and arm and at the right of the trachea, and the bullet was still in the neck. There was a pulsating tumor the size of a walnut behind the sternoclavicular joint on the right. No temporal pulse was felt; the radial was present on the right. There were contracture and paralysis of the right arm, particularly at the shoulder. The arm was painful and sensitive. Almost the entire brachial plexus was involved.

On October 4, with the patient under ether and chloform, a median incision of the neck was bisected by a horizontal one along the clavicle. The flaps were retracted. All veins were bleeding, with pulsation. The inner third of the clavicle was removed, and part of the sternum. A large adherent aneurysm was present. The innominate artery was exposed and ligated with silk thread. The pleura was opened by accident and packed. The right radial pulse ceased after ligation. The carotid was cut between the ligatures. The subclavian was ligated at its origin. The aneurysm was dissected out. The jugular and subclavian veins were ligated. The wound was closed with two gauze drains.

On the first day after operation, cough and pleuritic pain developed. The drains were removed with much bloody discharge. The right pulse was weak. On the fourth day, there was some cyanosis of the hand. On the sixth day, the

61. Myles: A Case of Ligature of the Innominate Artery, *Dublin J. M. Sc.* **124**:474, 1907; A Case of Ligature of the Innominate Artery, *Tr. Roy. Acad. Med., Ireland* **26**:278, 1907-1908.

62. Herzen: Ueber ein Fall von Unterbindung der Art Anonyma, *Deutsche Ztschr. f. Chir.* **104**:241, 1916.

stitches were taken out. There was slight inflammation. Bronchopneumonia developed in the right lung. On the eleventh day, there was general urticaria. The wound was closed on the seventeenth day, and on the twenty-first day the patient was discharged. Three months later the right arm was paralyzed, the right pulse was absent and the aneurysm was healed. In February, 1909, the brachial plexus was operated on with partial return of function.

CASE 64⁶³ (surgeon, Kimura, 1908).—A patient, aged 46 years, was admitted to the hospital in September, 1908, and operated on for popliteal aneurysm. On October 12, a pulsating tumor, the size of a hen's egg, was found in the neck behind the right sternomastoid.

On November 20, with the patient under chloroform, an incision was made at the inner margin of the sternomastoid. The carotid was exposed, and the aneurysm was found to be of the bifurcation. The subclavian artery was ligated with two silk threads, and cut near its origin. The innominate was ligated and cut near the aorta. The common carotid, which had had a partial ligature placed on it, was then ligated tightly, and the aneurysm was partially removed.

On the first day after operation the patient was slightly hoarse; there were no motor or sensory disturbances, and no pulsation in the right radial artery. On the third day, the hoarseness disappeared; the dressing was changed. On the thirty-third day, the patient was discharged from the hospital. There were no disturbances of the brain or arm. Seventeen months after this, his general condition was good, except for slight difficulty in walking, resulting from the popliteal operation.

CASE 65⁶⁴ (surgeon, Ballance, 1909).—A white man, aged 35, was admitted to the hospital in 1909. He had a swelling at the right root of the neck, and this swelling increased in size. The right radial and the carotid pulsation were smaller than the left.

The first and second left costal cartilages, the inner end of the left clavicle and the left three fourths of the manubrium were removed. The aneurysm was near the bifurcation of the innominate. The origin of the vessel was normal. The tumor was ruptured as the ligature was passed. The innominate was plugged with a finger in the sac and ligated with two kangaroo tendon ligatures tied with a stay knot but not crushing the coats. The man died thirty hours later.

CASE 66⁶⁵ (surgeon, Sargent, 1909).—A woman, aged 67, was admitted to the hospital on Aug. 12, 1909; she had noted pulsation in the root of the right side of the neck for eight weeks. There were pain, loss of power in the right arm, dyspnea, occasional cyanosis and some precordial pain. On examination, there was a pulsating tumor above and lateral to the sternoclavicular joint. The right pupil was greater than the left. The right arm was weaker than the left. After three weeks' rest, the patient was better. She was seen by Dr. Ballance, and an operation was decided on.

On September 14, with the patient under chloroform, a median vertical incision was made. The anterior jugular was tied; the right half of the manubrium and part of the first costal cartilage were removed. The sternohyoid was separated from the tumor. The left innominate vein was exposed and pulled upward. The aortic arch and origin of the innominate artery were exposed and appeared normal.

63. Imai: Ein durch Extirpation geheilter Fall von aneurysm der Art. Anonyma, Deutsche med. Wchnschr. **39**:1147, 1913.

64. Ballance (footnote 53, second reference).

65. Sargent: Aneurysm of the Innominate Artery, Proximal Ligature, Recovery, Lancet **1**:1200, 1911.

The innominate sheath was opened and a ligature passed $\frac{1}{2}$ inch from the origin. Two thick floss ligatures were tied with a stay knot. Pulsation ceased. The carotid was tied through another incision at the cricoid cartilage with no. 2 silk. The wound was closed.

On the first day after operation the right side of the face and the arm were cold and pulseless. From the sixth to the ninth days, there was pulsation at the aneurysm. On the tenth day, weakness of the left arm and the left side of the face was noted. The patient was discharged at the end of three months with the facial weakness gone. In June, 1910 she was normal. No pulse was felt at the aneurysm, nor was there any weakness of the arm. The radial pulse was weak, but present. The pupils were equal. The patient died on Feb. 20, 1911, from bronchopneumonia and chronic nephritis.

Autopsy revealed pneumonia, pericarditis, chronic interstitial nephritis and arteriosclerosis. The aneurysm arose from the innominate artery; the ligature was half way from the aorta to the aneurysm and was represented by a groove and obliteration of the artery. No silk was found. The subclavian was obliterated half an inch short of the vertebral branch. The condition of the carotid could not be ascertained. The clots closing the vessels were inseparable from the walls. The collateral was through the vertebral, internal mammary, inferior thyroid and suprascapular arteries, all of which were enlarged.

CASE 67⁶⁶ (surgeon, Morf, 1911).—A white man, aged 55, was admitted to the hospital on May 20, 1911, with a history of pain for five or six years in the deltoid muscle and down the arm. While being treated by an osteopath six months before admission, there was pain in the right supraclavicular region. The next day there was a pulsating tumor the size of a pigeon's egg. On admission, it was the size of a hen's egg and pulsated.

On May 28, with the patient under ether, an incision 13 cm. long was made 6 cm. above the clavicle. The sternomastoid muscle was divided. The inner third of the clavicle was resected. The right carotid artery was found and followed down to the innominate. The aneurysm involved the second portion of the subclavian. The innominate was isolated by blunt dissection. Two heavy kangaroo tendon ligatures were placed and tied. One ligature was tied about the common carotid at its origin. Pulsation ceased at once in the aneurysm and in the right arm. The wound was closed. The operation lasted one hour. The patient was in good condition.

After operation, the arm was slightly elevated and wrapped in wool. There was no cerebral disturbance. There was considerable pain in the right arm for a few days. The aneurysm became hard and firm. There was a distinct pulse in the right radial in two and a half weeks. Pulsation was felt in the aneurysm in three and a half weeks. The hand and arm were stiff for three months. In 1917, there was occasional pain in the right arm. The aneurysm measured 6 by 5 by 4 cm. The wall was firm and strong, except for a small area 2 cm. in diameter. It increased only slightly in size. The patient refused further operation.

CASE 68⁶⁷ (surgeon, Ballance, 1911).—A white man, aged 43, was admitted to the hospital on Oct. 23, 1911, with a large pulsating swelling above the right clavicle, extending from the middle of the clavicle to the head of the bone and 2

66 Morf. Ligature of the Innominate Artery for Subclavian Aneurysm, Surg. Gynec. Obst. 25:526, 1917.

67 Ballance. A Case of Ligation of the Innominate Artery for Subclavian Aneurysm, Proc. Roy. Soc. Med., Clin. Sect. 5:99, 1912, footnote 53, second reference.

inches above the middle. The right radial pulse was feeble. The pulse in the carotid and in the temporals was equal on both sides. The right pupil was contracted. The larynx was normal. In a roentgenogram, the aneurysm was seen to obliterate the apex of the right lung.

On November 1, an oblique incision was made to expose the first part of the subclavian, and the aneurysm was found to involve this portion. The incision was continued to the midline to expose the innominate artery. The upper half of the manubrium was removed. The bifurcation of the innominate was low in the superior mediastinum. Two sutures of kangaroo tendon were placed around the innominate, which occluded without rupture, and were tied with a stay knot. The wound was closed.

After operation, pulsation ceased at once and did not return. There was no pulsation in the right arm, but it was never cold. At first there were numbness and tingling of the fingers of the right hand, and they were stiff. The right pupil was dilated for twenty-four hours; then it became contracted and remained so. The arm was massaged on the twelfth day, and the patient was up on the twenty-second. He was last seen one month after operation.

CASE 69⁶⁸ (surgeon, J. R. Morison, 1912).—A white man, aged 51, was admitted to the hospital with a pulsating swelling in the lower right side of the neck, extending from the midline to the deltoid. There was excruciating pain, with numbness and loss of sensation down the right arm, which was swollen and had enlarged veins.

On July 20, an incision was made along the anterior edge of the sternomastoid and out along the clavicle. The sternomastoid muscle was divided. An aneurysm was found to involve the second and third parts of the subclavian artery. The innominate artery was easily exposed and separated, except laterally, where it was adherent. A hole was accidentally made in the vessel because of disease. This was occluded with clip forceps. A thick silk ligature was then passed around the vessel below this opening. The vessel was occluded with thick silk ligatures, tied tightly above and below the opening. The right carotid artery was tied with thick chromic catgut. A piece of fascia lata from the thigh was tied about the vessels, and the wound was closed without drainage.

After operation, the pain disappeared. There was complete anesthesia of the right arm. Fourteen days later, the feeling returned. The wound healed by primary union. Six weeks later, a small bleb was opened, which drained serum; it closed two weeks later. When the patient was last heard of, in 1914, the condition of the arm had improved.

CASE 70⁶⁸ (surgeon, W. S. Halsted, 1912).—A colored man, single, aged 47, was admitted to the hospital on Oct. 18, 1912, with an aneurysm of the right subclavian artery of three and three-fourths years and eleven days' duration. The subclavian artery was ligated in July, 1909, by Mayo. The patient remained well until eleven days before admission, when the swelling was discovered again. There was a large tumor behind the inner end of the clavicle and the sternoclavicular joint, measuring 13 by 8.5 cm. No pulse was felt in the right axillary, brachial or radial arteries. The surface temperature of the right arm and hand was lower than that of the left. Function and sensation were normal. The right pupil was small and there was ptosis.

68. Morison, J. R.: Leaking Aneurysm of the Subclavian Artery: Ligature of the Innominate and the Right Carotid Artery, *Brit. J. Surg.* 1:725, 1914.

On November 7, the right innominate artery was ligated for subclavian aneurysm. A faint pulsation in the aneurysm had returned by the time the wound was closed.

After operation the aneurysm became smaller, and measured 5.5 by 4 cm. on the discharge of the patient. No circulatory embarrassment of the hand was noted. The surface temperatures were about the same. At the last report, on Dec. 24, 1912, the patient had improved.

It was thought that this aneurysm was at the site of the previous ligation, and that the first aneurysm was in the third portion of the subclavian artery.

CASE 71⁶⁹ (surgeon, C. A. Hamann, 1913).—A white woman, aged 68, complained of severe pain in the right shoulder and arm and a pulsating swelling above the clavicle. The pain was present for from four to six weeks, and the swelling for one week. On Feb. 6, 1913, an attempt was made to insert a wire.

On February 10, with the patient under ether, an incision was made along the anterior border of the sternomastoid and along the clavicle. The sternomastoid was cut. The aneurysm was found to be of the third part of the subclavian extending to the first part. Two inches of the clavicle were resected. The innominate artery was exposed. A heavy braided double silk ligature was passed around the vessel $\frac{1}{2}$ inch below the bifurcation and tied with an ordinary surgical knot. The coat of the vessel, which was atheromatous, gave way. Pulsation ceased at once. The common carotid was tied 1 inch from its origin with no. 2 chromic catgut. The wound was closed. A small drain was placed at the inner angle. The arm was wrapped in cotton.

After operation the wound healed by first intention. No pulsation of the sac was felt. There was no cerebral trouble. On June 29, little trace of the sac was felt, and there was no pulse in the radial or brachial arteries. Thirteen months after operation, the patient was in good health and working. No aneurysm or radial pulse was noted. There was slight paresthesia of the fingers and forearm. The blood flow reported by Stewart was as follows: On March 20, 1.5 Gm. per hundred cubic centimeters per minute in the right arm and 5.32 in the left, a ratio of 1:3.53; on March 21, 1.83 Gm. in the right arm and 6.38 in the left, a ratio of 1:3.48; on July 9, 8.26 Gm. in the right arm and 10.69 in the left, a ratio of 1:1.3

CASE 72⁷⁰ (surgeon, Thompson, 1914).—A colored man, aged 46, presented a large pulsating swelling of the axillary and supraclavicular spaces. For four days, his arm had been swelling. It showed a huge swelling with dilated veins and edema of the right arm. A constant boring pain in the hand and wrist was alleviated by raising of the shoulders. The radial pulse was absent. The heart was normal.

On June 23, 1914, a transverse incision was made 1 inch above the clavicle from the midpoint to the middle of the neck. The sternomastoid, sternohyoid and sternothyroid were divided. The carotids and the innominate were exposed; pressure stopped the pulsation in the sac. The innominate was ligated with narrow linen tape, two strips of tape side by side, with Ballance and Edmunds' stay knot.

69. Stewart: Blood Flow in Hands and Feet in Cases in Which Obvious Anatomical Differences Exist, *Arch. Int. Med.* **12**:678 (Dec.) 1913. Hamann, C. A.: Ligation of the Innominate Artery with Report of a Successful Case, *Ann. Surg.* **59**:962, 1914; Ligature of the Innominate Artery with Report of a Case, *Tr. Am. Surg. Assn.* **32**:445 and 483, 1914.

70. Thompson, J. E.: Ligation of the Innominate Artery for Cure of Subclavian Aneurysm, *Ann. Surg.* **61**:641, 1915.

After operation there were no cerebral symptoms. There were complete paralysis and anesthesia of the arm. However, there was slight pain in the arm and shoulder. On July 15, more pain developed. On July 18, a soft, fluctuant tumor was felt in the floor of the right axilla. On July 21, pus was aspirated. On July 22, the axillary abscess was opened with a large flow of pus and blood. On August 1, there was a profuse hemorrhage from this site, which was packed. On August 29, sudden coma developed, and the patient died.

Autopsy revealed marked anemia in the brain. The heart valves showed ulcerations. The innominate artery was 5.5 cm. long; its wall was healthy. The left carotid rose from it; 2 cm. below the bifurcation above the left carotid was the ligature. The lumen of the artery admitted a small probe. The carotid distal to the ligature was normal. The aneurysm contained a clot. The distal opening was sealed.

CASE 73⁷¹ (surgeon, Lessnoi, 1915).—The patient was admitted to the hospital in November, 1914, shortly after being shot through the right side of the neck. There was a pulsating swelling toward the midline the size of a plum. Compression stopped the pulsation and also the pulse in the right carotid artery. Severe headache was caused by this. The radial pulse was equal. The patient was emaciated but normal, except for the tumor. After the wound healed, pressure was applied.

Operation was performed in January, 1915, general anesthesia being used. The head was dependent. An incision was made along the outer border of the sternomastoid to the manubrium, and the sternomastoid was cut. In clamping some of the vessels, the vagus was apparently caught, and the pulse ceased until the clamp was removed. An aneurysm of the common carotid was found. In an attempt to ligate the carotid it was found that the innominate was tied, as the pulse in the radial and carotid stopped. The aneurysm was therefore of the innominate. Excision of the sac was impossible. The wound was closed in layers with a small drain inserted at the lower corner.

After operation healing was uneventful. The drain was removed on the second day. Immediately after operation, the patient complained of headache, vertigo, difficulty in swallowing and weakness in the right arm. The right side of the face was cyanotic and pale. These symptoms disappeared in a short time, and the aneurysm disappeared. The patient was in good condition on discharge, except for loss of the carotid and the radial pulse.

CASE 74⁷² (surgeon, C. A. Hamann, 1915).—A colored man, aged 25, was admitted to the hospital on May 6, complaining of pain in the right shoulder and right arm of three weeks' duration. At this time a small lump appeared below the right clavicle. The lump increased in size rapidly till it measured from 3 to 4 inches in diameter; it was probably a subclavian aneurysm. There was loss of power in the right forearm and hand. No atrophy or edema was noted. The blood pressure in the right arm was 110 systolic and 88 diastolic; in the left arm, it was 130 systolic and 70 diastolic.

On May 11, the inner third of the clavicle was resected. The vessels were normal at the site of the ligature. The innominate was ligated with no. 5 braided silk and the common carotid with no. 3 chromic catgut.

71. Lessnoi: A Case of Successful Ligation of the Innominate Artery, *Arch. f. klin. Chir.* **150**:280, 1928.

72. Hamann, C. A.: Ligature of the Innominate and Carotid Arteries for Subclavian Aneurysm, *Cleveland M. J.* **15**:221, 1916. Stewart: Studies on the Circulation in Man, *J. Exper. Med.* **22**:694, 1915.

After operation there was no cerebral trouble. The arm was warm. The wound healed by first intention, and the pain and weakness of the arm disappeared. Two months later the patient was in good condition. The tumor decreased in size and did not pulsate. The blood flow determinations were: three days before operation, 12.52 Gm. per hundred cubic centimeters per minute in the right hand and 6.36 in the left, a ratio of 2:1; eleven days after operation, 3.44 Gm. in the right hand and 15.38 in the left, a ratio of 1:4.47; seventeen days after operation, 4.76 Gm. in the right hand and 15.31 in the left, a ratio of 1:3.21; twenty-four days after operation, 4.86 Gm. in the right hand and 9 in the left, a ratio of 1:1.85; thirty-one days after operation, 8.55 Gm. in the right hand and 14.24 Gm. in the left, a ratio of 1:1.66. There was no pulse in the right hand at this time.

CASE 75⁷³ (surgeon, Hamann, 1916?).—A woman, aged 59, had an aneurysm of the innominate, carotid and subclavian arteries. At the time of operation, the aneurysm was fusiform, and the three great vessels were dilated to three times their normal size. The innominate was tied with heavy silk and the carotid with chromic catgut.

After operation the patient developed a left-sided hemiplegia. She died on the fourth day.

CASE 76⁷⁴ (surgeon, Coughlin, 1916).—A negro, aged 28, was admitted to the hospital on May 9, 1916, with an aneurysm of the right subclavian artery.

On May 18, with the patient under intratracheal ether, a midline incision was made from the upper margin of the clavicle downward for 4 inches. A transverse incision 1½ inches long was made at the upper and lower ends. The sternum and three upper costal cartilages of both sides were removed. The left innominate vein was exposed and drawn down. The innominate artery was exposed. An aluminum band was inserted, and the vessel was occluded one-half. The operation lasted one hour and fifteen minutes. There was considerable oozing on the right side of the incision.

Three weeks after operation, with the patient under local anesthesia, the incision was reopened. The innominate was tied just distal to the band, and the carotid was tied just below its bifurcation. Two years later the patient was living and cured of his aneurysm.

CASE 77⁷⁵ (surgeon, T. Sinclair, 1916).—A white man was shot in the lower part of the right side of the neck on Aug. 24, 1916. He bled profusely for thirteen hours. He reached the casualty clearing station on August 25 and recovered from shock, but showed profound anemia. Traumatic arterial aneurysm developed in the lower part of the common carotid, which increased in size until the fourteenth day, when it measured 4½ by 4 inches. The wounds were suppurating. The patient was becoming hoarse from pressure on the recurrent nerve, and his temperature varied from 100 to 101.8 F.

On September 8, vertical and horizontal incisions were made. The sterno-mastoid was cut, and 1¼ inches of the clavicle was removed. The innominate was found behind the middle of the manubrium. It was tied with a single no. 4 chromic catgut ligature. The wound was closed over a small drain, which was

73. Hamann (footnote 72, first reference).

74. Coughlin, W. T.: Removal of Portion of Sternum for Ligation of the Innominate Artery, *Surg. Gynec. Obst.* **26**:112, 1918.

75. Sinclair, T.: Ligation of the Innominate Artery for Traumatic Aneurysm of the Carotid, *Brit. M. J.* **1**:288, 1917.

kept in for forty-eight hours. The distal ligation was postponed because of the patient's condition.

The patient was discharged on September 16, eight days after the operation, with no infection. Three months after operation, examination showed no cerebral deterioration. These vessels in the right eye were slightly smaller than those in the left. No loss of vision or dizziness was present. The swelling had entirely disappeared. The pulse of the right radial and ulnar was absent. Some feebleness and stiffness in the hand were noted, probably due to prolonged disuse. Good pseudo-arthritis with the first rib gave motion to the arm and shoulder.

CASE 78⁷⁴ (surgeon, Coughlin, 1916).—A mulatto, aged 27, was operated on on Oct. 23, 1916, under local anesthesia. A median incision 4 inches long was made downward from 1 inch above the sternum. Three costal cartilages and the sternum were resected. When an attempt was made to pass a band behind the innominate artery, the vessel was ruptured, and the patient bled to death.

CASE 79⁷⁵ (surgeon, Makins, —).—The patient was admitted to the hospital three days after a wound in the right side of the neck. He was pale and anemic, with a brachial monoplegia. There was no radial pulse. He was rested for fourteen days, and at the end of this time the tumor began to increase in size rapidly.

The innominate was exposed through an incision along the sternomastoid muscle, and a clamp was placed on it. The clavicle was resected, and a superficial blood clot was cleaned out. The aneurysmal sac was opened. There was an alarming hemorrhage, which was controlled by pressure against the cervical vertebra. The subclavian artery was found to be divided, and the hemorrhage occurred from the central end. The subclavian vein had apparently been destroyed. The first part of the subclavian artery was tied. The clamp was removed from the innominate artery.

The patient died at the end of three hours as a result of shock and hemorrhage.

CASE 80⁷⁷ (surgeon, Makins, —).—The patient was wounded by a piece of shell which passed through the anterior border of the right trapezius muscle. There was marked hemorrhage at the time of the injury. Fourteen days later, there was a large subcutaneous swelling in the right side of the neck. This improved, and on the seventieth day operation was done.

An incision was made along the sternomastoid and along the clavicle. The sternomastoid was divided. The sac arose from the first portion of the subclavian artery and vein, and extended upward to the fourth cervical vertebra. The carotid and innominate arteries were exposed, and, owing to the injury to the first portion of the subclavian, a ligature was passed around the innominate and the third portion of the subclavian. The sac was dissected; during this process, it was opened by mistake. The innominate ligature was immediately tightened. The sac was found, dissected out and ligated off at its connection with the artery and the vein. The patient lost a considerable amount of blood. The wound was closed.

After operation, saline infusion improved the condition markedly. On the second day, there was a paralysis of the left arm, which disappeared on the fourth. The stitches were removed on the eighth day. From the seventh to twelfth days, there was discharge from the wound, which suggested an injury to the right lymphatic duct. The patient made an excellent recovery.

76. Makins, G. H.: *Gunshot Injuries to the Blood Vessels*, New York, William Wood & Company, 1919, p. 181.

77. Makins (footnote 76, p. 184).

CASE 81⁷⁸ (surgeon, Sauerbruch, —).—During the war, a small injury of the innominate artery was sutured by Sauerbruch. The patient died from suppurative mediastinitis five days later.

CASE 82⁷⁹ (surgeon, Halsted, 1918).—A colored man, aged 45, was admitted to the hospital on Jan. 28, 1918, with an aneurysm of the right common carotid artery of three years' duration. Pain was felt in the right sternoclavicular region. He had difficulty in swallowing. The right pupil was small, and there was slight ptosis. Behind the clavicle was found a tumor, 6.5 by 4.5 cm. The heart was normal.

On January 28, the innominate artery was ligated. The clavicle, part of the sternum and part of the first rib were resected.

The pulse was noted at the wrist in the afternoon of the operation, becoming countable at 8 p. m. A definite pulse was felt in the carotid and in the aneurysm, also in the wrist and the temporal artery, the day after operation. The blood pressure in the left arm was 122 systolic and 75 diastolic, and in the right arm 90 systolic and 67 diastolic. Ten days after operation, no pulse was felt in the aneurysm or the carotid; a good pulse was felt at the wrist. When the patient was discharged, the aneurysm was pulseless; the right pupil was small, and there was ptosis. A good pulse was felt at the wrist and in the temple. No cerebral disturbances or trophic or sensory changes were noted. On March 25, the patient returned to the hospital with a pulsation and an increase in the size of the tumor. The carotid artery was pulseless, but felt like a cord. The pulse in the radial and temporal was still felt. The blood pressure in the left arm was 105 systolic and 65 diastolic, and in the right arm, 83 systolic and 70 diastolic. On April 9, the common carotid was ligated with a band and ligature. The common carotid was small, thick-walled and contained no pulse, yet at the conclusion of the operation no pulse could be felt in the aneurysm. There was no return of pulsation in the aneurysm after this. On April 28, the patient was well. On May 6, the aneurysm was 5 cm. in diameter, and pulseless. The patient was last heard of on May 15, 1922, by letter. He works hard and shows no evidence of aneurysm. The aneurysm has disappeared, except for a small cord the size of the little finger.

CASE 83⁸⁰ (surgeon, M. Reid, 1918).—A white man, aged 45, with aneurysm of the innominate artery of two years' duration was admitted to the hospital on June 6, 1918. Severe pain was felt in the hand and occiput for two years before the swelling appeared. Ten months before admission, he had had the carotid and subclavian tied distal to the aneurysm, but with no relief. The pupils were equal. An aneurysm was eroding through the sternoclavicular articulation.

On June 15, an attempt was made to ligate the innominate artery for the aneurysm. The patient died before the ligature could be placed. Death was apparently due to pulling on the arch of the aorta. The innominate artery at its junction with the aorta was bigger than the aorta and was very sclerotic.

CASE 84⁸⁰ (surgeon, Halsted, 1918).—The patient had received a bullet wound in the right side of the neck above the sternoclavicular joint on Sept. 12, 1918. He walked one mile. Immediate swelling of the neck and hoarseness of the voice occurred, and there was hemoptysis for three days. He entered the base hospital on September 16, with a stiff neck, difficulty in swallowing and a weak and low voice. There was diffuse ecchymosis. Slight pain was felt.

78. Krampf: *Beitrage zur Gefaschirurgie*, Deutsche Ztschr. f. Chir. 199:152, 1926.

79. Halsted, W. B.: *False Aneurysm of the Innominate Artery*, Surg. Gynec. Obst. 30:529, 1920.

Operation was performed on September 26. The patient was asphyxiated at the time he entered the operating room. An incision was hurriedly made over the most prominent part. There was a violent hemorrhage. The index finger inserted in the wound found the opening on the superior surface of the innominate artery. Clots were evacuated. The hemorrhage was controlled by a finger. The inner part of the clavicle and the upper part of the sternum were resected. The opening in the vessel was sutured with no. 0 chromic catgut.

The patient was up and around on November 10. He made gradual improvement.

CASE 85⁸¹ (surgeon, C. A. Ballance, 1918).—A white woman, aged 60, was admitted to the hospital in December, 1918, with a pulsating tumor the size of an orange in the right side of the lower part of the neck, above the sternum and clavicle, extending to the superior mediastinum. Roentgen examination showed a normal aorta. The right arm, the carotid and the temporal pulses were weaker than the left.

On December 31, an incision was made in the midline of the manubrium meeting a transverse incision. Both flaps were dissected upward. The wall of the aneurysm was found to be weak. The left sternomastoid and the left upper half of the manubrium were cut; the sternoclavicular joint and the first costal cartilage were removed. The left innominate vein was exposed, and the origin of the innominate artery was found. It was ligated with two strands of kangaroo tendon without rupturing the coats, and tied with a heavy stay knot. The wound was closed in layers.

After operation, there was primary union. The right arm was cold and useless at first with no pulse and slight motion in the fingers. There was slight improvement at the end of six weeks, but no pulse. The aneurysm became small and solid. In January, 1921, two years after operation, dyspnea and palpitation were present. A small, hard mass could be felt behind the clavicle. There was no aneurysm. The right arm had recovered its usefulness. The right pulse was equal to the left. The patient was admitted to the hospital on December 12, with a cardiovascular breakdown, and died on June 6, 1922, with a large infarct of the lung.

Autopsy showed the aneurysm gone and the artery obstructed. A fibrous mass was left attached to the distal part of the artery.

CASE 86⁸⁰ (surgeon, Juckelson, 1919).—The patient, aged 30, had been injured in the outer margin of the left side of the neck with a dull instrument some time before admission. On examination, a pulsating mass was seen near the midline, adherent to the clavicle. There was ptosis on the left. A diagnosis was made of aneurysm, either of the carotid or of the subclavian artery on the left.

On April 14, 1919, an incision 18 cm. long was made along the right sternomastoid muscle. The aneurysm burst. The bleeding was stopped with the finger. The inner end of the clavicle and of the sternum were removed. The source of the bleeding was traced down to the artery and the first part of the common carotid was found to be involved. There was considerable fibrosis of the tissues. The innominate artery was ligated twice, 1.5 cm. apart. The finger was removed, but bleeding continued from the distal side. The common carotid and the subclavian were also ligated. The sac consisted of two parts. The one projecting to the left side and filled with clot did not pulsate. Part of the sac was removed, but it was necessary to stop, and the remainder was packed. Removal of pressure on the trachea improved the patient's breathing.

80. Juckelson: Case of Ligation of the Innominate Artery, *Zentralbl. f. Chir.* 13:687, 1925,

The postoperative course was uneventful. The wound healed where it was sutured excellently. Except for a left-sided headache, there were no brain symptoms. Slight paleness of the right arm was noted. The radial pulse did not return. The patient was discharged two weeks after operation with a granulating wound. Five years and eight months after this he was in good health, and did not have an aneurysm.

CASE 87⁸¹ (surgeon, Hertzler, 1922).—The patient was injured on Dec. 25, 1921, by a gunshot wound from the top of the sternum to the right shoulder. The bullet was removed from the right shoulder. Immediate paralysis of the right arm developed. The pulsating mass appeared in the right supraclavicular fossa. The mass was the size of an orange. A diagnosis of aneurysm of the right subclavian artery was made.

On Nov. 24, 1922, with the patient under ether, an incision was made along the right clavicle. The sternomastoid was resected. A large sac was found extending to within 1 cm. of the innominate. The innominate was ligated with double linen thread, just below the bifurcation. The wound was closed with an iodoform gauze drain. The patient was discharged one month later, after uneventful recovery. There was no pulsation in the aneurysm; no pulse was felt in the right arm. The paralysis was better. Ten days later, pulsation returned in the sac. On Jan. 13, 1923, with the patient under local anesthesia, the vertebral and common carotid were ligated. Pulsation did not cease entirely. Recovery was uneventful. On June 16, an aneurysm the size of an egg was still present and pulsating. Pulsations were present in the right radial and ulna.

CASE 88⁸² (surgeon, Holman, 1922).—A white man, aged 25, on Oct. 22, 1922, sustained a pistol shot in the right clavicular region. A profuse hemorrhage was easily controlled by slight pressure. Several days later, he noticed a small tumor about 2 cm. above the small healing wound. It progressed slowly for five weeks, and rapidly after that. After the accident, he noticed violent beating of the heart when he made the slightest effort. He was admitted to the hospital on November 29, with a large pulsating swelling extending from the midline to the anterior border of the trapezius. There was a small scar at the site of the wound. The bullet was near the apex of the left lung. Thrill and murmur were continuous. Deep pressure above the center of the clavicle caused both to disappear and caused a temporary slowing of the pulse. Release of pressure caused a momentary rapid beating of the heart. The blood pressure in the left arm was 108 systolic and 62 diastolic. After compression, it rose to 114 and then fell to 108. On release of pressure it fell to 102 and recovered immediately to 108. On release of the pressure, the diastolic pressure fell to 48, recovering within a few seconds to 62. The blood pressure in the right arm was consistently from 4 to 8 mm. less than in the left. The superficial veins of the forearm were more prominent on the right than on the left. There was no cardiac enlargement. A diagnosis of varicose aneurysm of the subclavian vessels with a small communication was made. Operation was planned to expose the subclavian vessels and to ligate with quadruple ligature.

In December, 1922, along the clavicle to the sternum, a horizontal incision was made which bisected a median vertical incision. Two thirds of the clavicle was

81. Hertzler, A. E.: Traumatic Aneurysm of the First Part of the Subclavian Artery, *S. Clin. N. Amer.* **3**:1507, 1923.

82. Holman, E.: Surgery of the Large Arteries with Report of a Case of Ligation of the Innominate Artery for Varicose Aneurysm of the Subclavian Vessels. *Ann. Surg.* **85**:173, 1927.

resected, and the clavicle was slightly eroded. When the clavicle was removed the aneurysm burst, sending out a flow of arterial and venous blood under great pressure. This was stopped by pressure with the thumb, and the clavicle and sternum were resected. The innominate artery was exposed and a tape ligature was placed around it with a small length of rubber tubing to prevent crushing the wall. The common carotid was exposed and occluded in a similar manner. The pulsation of the swelling ceased, and the operation could be continued. Rows of silk sutures closed the sac. The carotid ligature was released with bleeding. The innominate ligature was released with return of pulsation and bleeding. Therefore permanent tape ligature occluding the innominate artery, but not crushing it, was applied. The wound was closed without drainage. The patient was in a poor condition.

The subclavian vein was probably included in the deep sutures, which explained the cessation of thrill and bruit. Marked pallor and absence of perspiration on the right side of the face were noted immediately after operation. Right radial paralysis returned eight hours after operation. There was some numbness of the right arm and hand, which disappeared in forty-eight hours. Four days after operation, the neck was normal in size, and there was no pulsation. Thirteen and twenty days after operation, a small opening along the line of incision was made to evacuate old fluid blood. At discharge, a good pulse could be felt at the wrist, and the right carotid and temporal vessels felt full and firm. The veins in the left arm collapsed 4 degrees above horizontal, and in the right arm 20 degrees above horizontal. This was interpreted as indicating that the subclavian vein had been occluded at operation. The blood pressure in the right arm was 76 systolic and 74 diastolic, and in the left arm 120 systolic and 76 diastolic. One year after operation the right arm was still weaker than the left but was gradually improving. There was no perspiration on the right side of the face. The right side of the face and the right arm were colder in cold weather. Slight enophthalmos was present. The pupils were equal. The neck was normal. The right carotid and the radial pulse were weak and slightly retarded. There was no atrophy. The blood pressure in the left arm was 118 systolic and 92 diastolic, and in the right arm 90 systolic and 70 diastolic.

CASE 89 (surgeon, Greenough, 1924).—This case was reported in full in the beginning of this article.

CASE 90 ⁷³ (surgeon, Sauerbruch, 1925).—On Jan. 19, 1925, operation was performed on a partly calcified tumor reaching into the upper thoracic aperture. The inferior and superior thyroid arteries were ligated. In dissecting the lower pole, a severe arterial hemorrhage occurred. The vessel was inaccessible, so compression controlled the hemorrhage. Part of the manubrium was resected, and the bleeding was found to come from a short thyroidea ima springing from the innominate just before bifurcation. Rubber clamps were applied to the innominate. With fine button silk sutures, a longitudinal suture 1 cm. long was made of the contused part of the innominate, including the origin of the thyroidea ima. When the clamps were removed there was no hemorrhage, although the artery was somewhat narrowed. The operation proceeded; the wound was closed in the usual manner. The postoperative course was uneventful.

CASE 91 ⁸³ (surgeon, E. R. Flint, 1927).—A white man, aged 37, had a bullet wound at the base of the right side of the neck nine years before admission to the

83. Flint, E. R.: Ligature of the Innominate Artery for Innominate Aneurysm, *Brit. M. J.* 1:979, 1928.

hospital. After the wound healed two swellings were left, and the voice remained husky; there were frequent attacks of pain in the neck, headache and vomiting. There had been transitory loss of vision in the right eye two years before. Two weeks before admission the swelling over the manubrium had increased rapidly with an increase in pain and difficulty in swallowing; the right pupil had become smaller than the left. In the right radial and carotid arteries there was only weak pulsation. There was paralysis of the recurrent nerve.

On Jan. 24, 1927, the manubrium sterni was removed after the sac had been carefully dissected off. The aneurysm of the innominate was found at the bifurcation. There was $\frac{1}{2}$ inch of normal artery proximal to this. A ligature of no. 2 chromic catgut was passed and tied sufficiently tight to approximate the walls. The recent symptoms had probably been due to a leak which was found in the upper right side of the sac. The clot was turned out. There was vigorous bleeding from the subclavian artery. The inner side of the sac was sutured at this point and the hemorrhage stopped. The sac was packed, as it was impossible to remove or obliterate it.

The wound took some weeks to heal owing to the packing. The right arm was useless at first, but later improved and was stronger; it remained pulseless. At the end of six months, the patient was well. There has been no recurrence of aneurysm. The patient still had a husky voice and vision was limited to the central area.

SUMMARY

A case of successful ligation of the innominate, carotid and subclavian arteries is reported.

Ninety-one cases of operation on the innominate artery, 75 per cent of which were ligation, are collected from the literature and summarized.

The total mortality after ligation is 56 per cent.

The mortality in the last 25 cases is 16 per cent.

Sufficient exposure by bone resection is advisable in operations on the innominate artery.

The innominate should be ligated with strong material applied with a force between 3 and 10 pounds (1.4 and 4.5 Kg.), and a stay knot used and the artery severed.

The wound, if uninfected, should not be drained.

If the operation is for aneurysm, distal as well as proximal ligation should be done and the sac extirpated or destroyed.

It is more advisable to ligate the subclavian artery than the carotid.

Ligation of the right innominate vein should benefit the circulation in the brain and the upper extremity.

The operation is justifiable, and if contemplated should be done early.

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ABSTRACT OF DISCUSSION

DR. JOHN ALEXANDER, Ann Arbor, Mich.: A year ago I had occasion to perform decompression on the superior mediastinal organs for suffocation from a slowly dissecting ruptured aneurysm of the aortic arch. Good, strictly extrapleural exposure of the arch of the aorta, the innominate artery and vein was obtained under local anesthesia after resecting the second right costal cartilage and anterior end of the second rib, the lower part of the first costal cartilage and the upper part of the second, and the right half of the manubrium; the internal mammary vessels were ligated and divided, and the pleura rolled laterally and posteriorly. An innominate artery that was normal at its origin might have been ligated without great difficulty. Another operation on the right superior mediastinum also demonstrated the usefulness and relative simplicity of this approach.

DR. EMILE HOLMAN, San Francisco: If you are encouraged by Dr. Greenough's interesting presentation to ligate the innominate artery, I think that you would be wise to ligate the innominate vein also.

I recently operated on a patient with a subclavian aneurysm. The subclavian, the carotid and the axillary arteries were ligated distal to the aneurysm, and I also ligated the innominate vein. Gangrene was averted, I feel, by the ligation of the vein. In case you are prompted to proceed with multiple ligations, I think that the innominate vein should be ligated also. It is not quite clear as to whether Dr. Greenough ligated the carotid and subclavian distal to the aneurysm or proximal to it.

DR. JAMES GREENOUGH: The arteries were ligated distal to the aneurysm.

The subclavian approach from behind is, of course, simple in the operation of thoracoplasty of the first rib, but one is doing a great deal of operating for another purpose. I think that if one is going to ligate only the subclavian or the innominate, the anterior approach would be easier.

The anatomy of the origin of the innominate, and of the bifurcation varies considerably, and I think that this variation determines the question of whether the thorax has to be entered or not.

OPERATIONS AND DEMONSTRATIONS OF CASES IN BARNES HOSPITAL

1. THORACOPLASTY AND PHRENICECTOMY

EVARTS A. GRAHAM, M.D.

AND

DUFF S. ALLEN, M.D.

ST. LOUIS

CASE 1.—*Phrenicectomy for Bronchiectasis of the Left Lower Lobe by Dr. Graham.*

A woman, aged 28, was admitted to the hospital on Nov. 13, 1928. Her chief complaint was bloody expectoration of fifteen months' duration, most marked during the three weeks previous to admission. She had always been weak and susceptible to colds. She had whooping cough at the age of 5 years and mumps at the age of 12. Her menstrual history was negative. She had been married for eight years, but there had been no pregnancies.

The onset of the present illness occurred at the age of 13, when the patient suffered from a cold which was associated with a purulent discharge from both ears. Her cough was then productive of grayish-white sputum. She was able to be up and about, however, and it was not until the age of 16 that she contracted what was considered to be typical pneumonia of the left lower lobe. Shortly after her recovery from this condition she had her tonsils and adenoids removed and from this time on she was no longer troubled with earache or discharging ears. Her cough disappeared and did not return until she suffered from another attack of pneumonia at the age of 18. The pneumonia also apparently cleared up and she was well until the age of 21 when the cough and expectoration returned as before. Since then she has been gradually losing weight. During the fifteen months previous to her admission to Barnes Hospital she coughed up blood in amounts up to a cupful.

On admission, the blood count showed a slight secondary anemia, and a leukocytosis of 13,000. The differential count was normal; the sputum showed no tubercle bacilli. The Wassermann and Kahn tests of the blood were negative. Physical signs and roentgen examination indicated a lesion in the left lower lobe considered to be bronchiectasis (fig. 1). Because of an alarming hemorrhage, bronchoscopy was not performed and patient received pneumothorax treatment on the left side. She is still receiving this treatment and has undoubtedly improved.

She was readmitted to the hospital on April 24, 1929, because it was thought that a phrenicectomy might improve her condition further by elevating the lower lobe and thus making the dilated bronchi more horizontal and less dependent. This operation was performed on April 25. With the patient under procaine hydrochloride infiltration anesthesia an incision was made parallel to and about one-half inch (1.27 cm.) above the left clavicle. The sternocleidomastoid muscle was split in the direction of its fibers immediately over the scalenus anticus muscle. The phrenic nerve was found in its normal position on the anterior border of the latter muscle. The nerve for a distance of about 12 inches (30.4 cm.) was twisted out of its bed. A little nitrous oxide was given to the patient while the nerve was being twisted.

The patient's diaphragm was observed to be paralyzed on the following day, and since then it has risen further. Pneumothorax treatment is being continued, and she has undoubtedly improved appreciably. It has been thought advisable to treat the nasal sinuses, but in this instance it was felt that the other procedures noted could perhaps be performed first with advantage.

CASE 2.—*First Stage Extrapleural Thoracoplasty for Tuberculosis*, by Dr. Graham.

A woman, aged 39, was admitted to Barnes Hospital on July 5, 1928. Her chief complaints were productive cough, weakness and vomiting.



Fig. 1.—Bronchiectasis of the left lower lobe demonstrated by injection of iodized oil. The oil seen in the extreme lower portion of the left side is in the stomach and not in the lung.

At the age of 15 the patient suffered from pain in the left side of the chest but it was not until 1922 that she had what has been described as an attack of influenza. She then began to suffer from elevation of temperature. Tubercle bacilli were found in the sputum at that time. Since then she has also had frequent attacks of pain in the left side of the chest, productive cough and fever, and has been losing weight. She has had hemorrhages on several occasions and of late some vomiting.

On admission, the leukocyte count was 18,600; physical signs verified the diagnosis of left-sided chronic pulmonary tuberculosis with cavitation (fig. 2). She was discharged from the hospital on July 17, 1928, and was readmitted on September 28.

Her condition on this occasion did not show any obvious improvement and it was thought advisable to start pneumothorax treatment. The sputum was negative. The first pneumothorax treatment was given on October 2, and this form of treatment was continued at intervals but not with any marked improvement since there were several adhesions extending from the midportion of the lung to the wall of the chest.

Cauterization of the pulmonary adhesions through a thoracoscope was therefore attempted on October 29, but this was only partially successful since many of the adhesions were broad and of the type that is best left alone. This procedure was not followed by any particular discomfort and the patient was discharged on November 30. She was readmitted to the hospital on Feb. 27, 1929.



Fig. 2.—Left unilateral pulmonary tuberculosis before operation.

Twelve inches of the phrenic nerve on the left side were removed on March 2. This operation was followed by some rise of the diaphragm but it was obvious that a thoracoplasty was indicated. It was performed in two stages: the first one on April 25 when portions of four lower ribs from the transverse process to the midaxillary line were removed. The patient stood this operation well but not until May 8 were the remaining ribs, including the first, removed. The postoperative course was satisfactory. Suppurative otitis media developed, but this was apparently not of a tuberculous nature. She was discharged on June 16, much improved (figs. 3 and 4). At her most recent admission on September 29, the following notes have been made: The patient feels well and looks well. She has gained in strength, is able to do light work and no longer has gastro-intestinal discomfort. She is free from cough and expectoration and is up and about.

CASE 3.—*Thoracoplasty for Chronic Suppurative Empyema*, by Dr. Graham.

A man, aged 65, was admitted to Barnes Hospital on Feb. 6, 1929. He complained of pain in the left side of the chest, loss of weight (from 145 to 129 pounds), 16 pounds (7.8 Kg.) in two months, and of weakness. He had pneumonia in 1903, and questionable pleurisy in 1907. The present illness began on Dec. 1, 1928, when the patient was taken ill with a chill, pain in the left side of the chest and coughing. He was then considered to be suffering from pneumonia. He was taken to a hospital, where he remained for eight weeks. His course in this hospital was not suggestive of a simple pneumonia and because of failure to improve he came to Barnes Hospital on Feb. 6, 1929, suffering from the foregoing complaints.

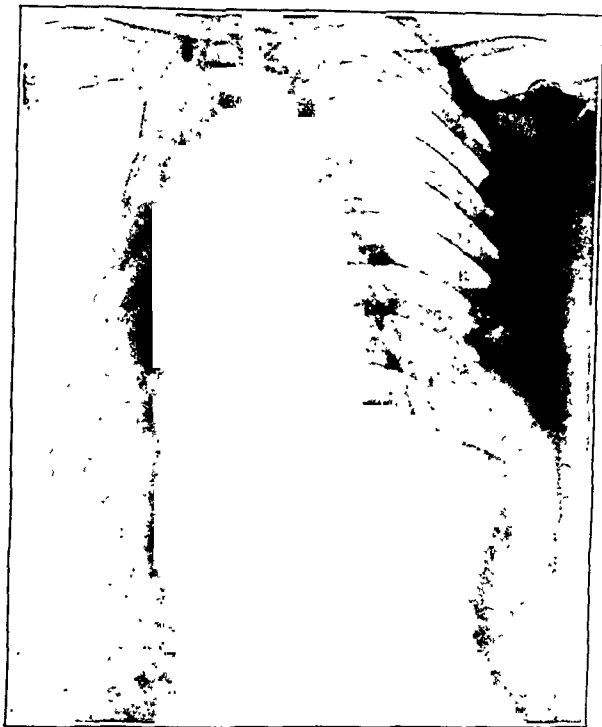


Fig. 3.—The same case as figure 2 after the completion of the thoracoplasty. A thoroughly satisfactory collapse of the left side was obtained by the operation.

The physical signs and roentgenograms showed a left-sided encysted empyema (figs. 5 and 6). The patient's prostate was slightly suggestive of a malignant condition. No tubercle bacilli could be demonstrated in his sputum. On February 12, a portion of the fifth left rib was resected between the posterior and anterior lines. About 250 cc. of thick, odorless pus escaped. There were also several large masses of fibrin. The parietal pleura was not so much thickened as would be expected in an ordinary empyema. A piece of the pleura was removed for microscopic examination and was subsequently reported as chronic inflammatory tissue. Two large tubes were inserted for drainage. Into each was passed a Dakin tube for irrigating purposes. The postoperative course was fairly satisfactory, but the cavity never became completely obliterated.

Because of the persistence of a small cavity and some bronchial fistulas, the patient was again operated on on April 25. The incision was carried around the old sinus. The old empyema cavity was found to extend backward and both upward and downward along the vertebral gutter. Two more ribs and thickened parietal pleura were resected in order to take off part of the roof of the cavity. It was not certain whether the foregoing procedure would suffice, but it was thought unwise to prolong the operation any longer because of the patient's advanced age. A piece of pleura was again removed for examination and showed nothing but chronic inflammation. The postoperative course was satisfactory and the patient would have been discharged much earlier than June 25, had it not been for the fact that he was suffering from a frequency of urination due to prostatic hypertrophy.

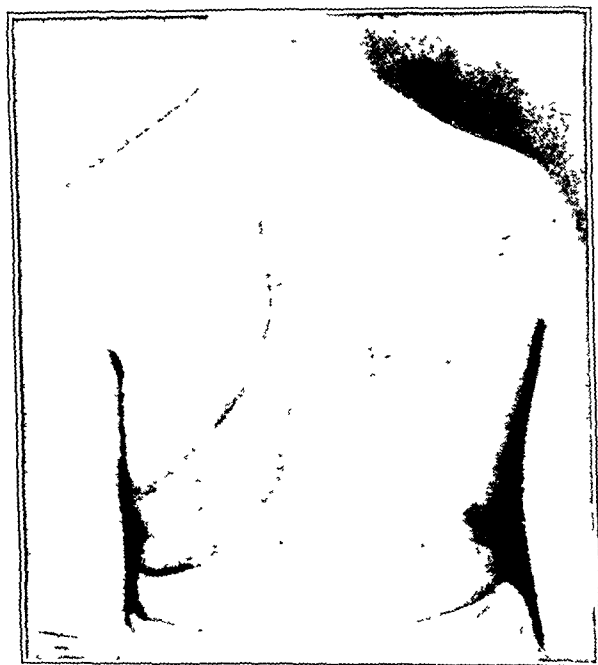


Fig. 4.—The same patient showing healed incisions. Sometimes we perform both stages of a thoracoplasty through the same incision. For the second stage the first incision is reopened. Lately, however, we have been employing two incisions as shown in the illustration. These have been retouched on the photograph to make them more visible.

It is to be noted that an injection of iodized oil demonstrated the presence of a left-sided bronchiectasis of the saccular type so that the possibility that one of these sacculations had broken into the pleura could not be excluded.

The patient's wound healed solidly, and in September he reported that he had no symptoms attributable to his old empyema.

CASE 4.—Thoracoplasty for Tuberculous Empyema, by Dr. Allen.

A man, aged 48, was admitted to Barnes Hospital on April 24, 1929. The onset of the present illness was somewhat indefinite. In February, 1928, he complained of night sweats and fever but did not suffer from cough or hemoptysis. He then entered the City Hospital only to be transferred to Koch Hospital where he remained for one year and where his condition was diagnosed as chronic pulmonary



Fig. 5.—Old encysted empyema.



Fig. 6.—Injection of iodized oil through the external fistula in the same case as in figure 5.

tuberculosis of the right lung. He began to suffer from pain in the right side of the chest which necessitated a resection of the ribs in September, 1928, when a diagnosis of right-sided empyema was made. He returned to the City Hospital in February, 1929, because of cough, expectoration and discharging sinuses of the chest. The sinuses, however, were troubling him more than the cough and expectoration. A thoracoplasty was performed in several stages; the first at the City Hospital, the second on April 25, and the last stage on June 8. The intervals between the various stages were long because the postoperative course in every instance was rather stormy.

The patient is continuing his rest cure at the present time. He feels much improved and is no longer troubled with discharging sinuses.

2. CLINIC DEMONSTRATIONS

JACOB J. SINGER, M.D.

AND

EVARTS A. GRAHAM, M.D.

ST. LOUIS

It is our desire to present a series of cases which illustrate not only certain interesting conditions but also certain details of our methods of handling such cases here. We also wish to emphasize the importance of an approach to all cases of chest conditions according to a plan of cooperation between the medical and surgical services. For nearly ten years we have been associated in the organization and development of a chest service for this group of hospitals. We meet almost daily and discuss patients who may possibly have any surgical conditions of the chest. The mutual cooperation of those with a medical and those with a surgical point of view on many of these cases is most helpful. In any large general hospital there are many patients who too often remain in the medical wards and are not given the benefit of the possibility of surgical help. The organization of a chest service for diagnosis and discussion of this group of patients will do much to increase the amount and improve the quality of thoracic surgery at that institution.

ABSCESS OF THE LUNG

The first group of cases which we shall present is a series of abscesses of the lung. We have recently noted a sharp decline in the number of such cases and also of bronchiectasis. It is interesting to note on inquiry that many others have also made this observation. Whether the warnings of this association of the dangers of tonsillectomy performed under general anesthesia are responsible for this decline, we do not know. Probably other factors are operating, such as no repetitions of any epidemic of respiratory disease corresponding to the influenza epidemics of 1917 and 1918.

We have consistently attempted to treat our patients in a conservative way, waiting for several weeks before employing any surgical procedure. We, like others, have found that many abscesses, although very large, will heal in time merely by the use of postural drainage.

The abscesses in many patients who seem suitable subjects for bronchoscopic drainage, according to the report of our leading bronchoscopists, have been healed in a few weeks without it. For this reason we are probably more conservative in our opinion of, and perhaps even more skeptical about, the therapeutic value of the bronchoscope in this type of case than are many others. As a matter of fact, in our experi-

ence the type of case which responds most readily to bronchoscopy is the same as that which also responds best to postural drainage or to methods of collapse.

In almost no case do we resort to surgical measures until after trial of the comparatively simple methods of postural drainage alone or of that combined with pneumothorax when the latter is possible. We also agree with Miller and Lambert and others that it is very dangerous to induce surgical drainage during the acute stage of a pulmonary abscess at a time when it is necessary to traverse a large zone of edematous lung tissue in order to reach the abscess.

CASE 1.—Acute Abscess of the Lung Treated with Postural Drainage.

G. C., a man, aged 49, was admitted to the hospital on June 7, 1927, complaining of chills, fever, cough, mucopurulent expectoration and general malaise. The onset of symptoms was six days after a tonsillectomy, three weeks previous to his admission to the hospital. Physical and roentgen examinations revealed the presence of an annular cavity about 5 cm. in diameter in the region of the hilum of the right lung. This cavity showed a fluid level which shifted with change of position. The patient's sputum contained many spirochetes.

Treatment consisted only of postural drainage and six intravenous injections of neoarsphenamine at weekly intervals. Improvement was gradual but definite. After two months the shadow at the site of the abscess had almost entirely disappeared, and the patient has been entirely free from all symptoms since then, nearly two years (figs. 1 and 2).

This case illustrates in a striking manner the healing after simple treatment of a large acute abscess of a kind which is usually subjected to more formidable measures, such as surgical drainage, pneumothorax or even bronchoscopic drainage.

Surgical drainage is instituted only after a trial of various medical means including bronchoscopy, pneumothorax, postural drainage and intravenous medication of arsenic in the cases of spirochetal infection. We usually wait from five to six weeks in acute cases before considering surgical drainage, and we wait even longer if the progress with more conservative measures seems satisfactory. In the chronic cases the location of the abscess, the presence of adhesions and the general condition of the patient determine our course. As a result of the more extensive use of conservative measures in the treatment of acute pulmonary abscess during the last five years we now operate much less often in such cases than formerly.

In spite of all methods of treatment, however, some cases become chronic and refractory. The following case is illustrative of the type in which we think the operation of cauterizing pneumectomy is indicated. Probably no other method known at present would have been so safe and at the same time so effective in ridding this patient of multiple abscesses.

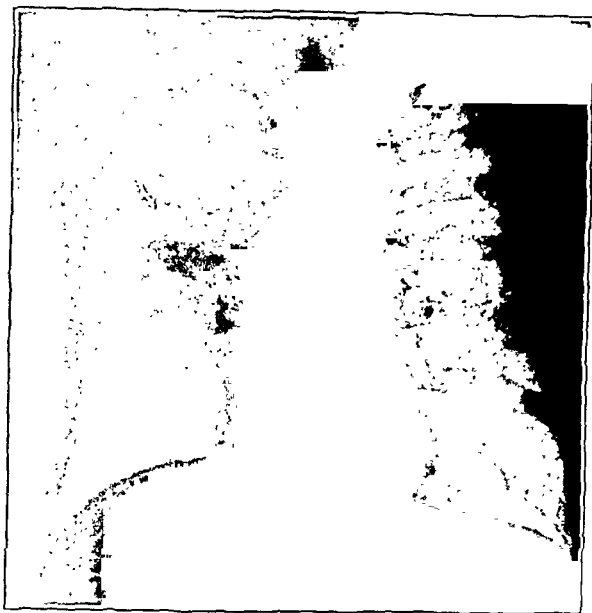


Fig. 1.—Abscess cavity in the right lung in case 1 of clinic demonstrations.



Fig. 2.—Same case as in figure 1, seven months later, showing complete healing of the abscess cavity produced only by rest and postural drainage.

CASE 2.—*Cautery Pneumectomy for Chronic Multiple Abscess of the Lung.*

L. P., a man, aged 28, was admitted to Barnes Hospital on Sept. 13, 1926. His complaints on admission were cough, expectoration and weakness. Five months previously to admission his tonsils were removed elsewhere under ether anesthesia. Three days after the tonsillectomy he noticed a slight dry cough which continued to increase in severity and became very productive. His appetite became poor, and he lost 18 pounds (8.2 Kg.) in weight during the three months before admission. He also complained of slight pain under the right shoulder and of fever during his entire illness.

On admission, physical examination showed that all the physical signs in the chest were localized to the region of the right hilum where breath sounds were diminished. An injection of iodized oil showed no direct evidence of any abscess cavities.

Artificial pneumothorax with repeated refills was performed. The lung showed good collapse, but there was only slight temporary decrease in the cough and expectoration following each pneumothorax. After twelve weeks of this conservative treatment, the patient did not show satisfactory improvement. About five weeks previous to his operation, for no apparent reason, the clinical picture of an embolus of the brain developed. The patient was drowsy, stuporous, and at times comatose for more than a week. He had weakness of his left facial muscles and slight twitchings. He was quite disoriented. This condition cleared up entirely after ten days, and on December 20 three ribs were resected. On December 31, a cautery pneumectomy was performed and a great many small pus pockets were encountered. The postoperative course was complicated by a right-sided empyema which was drained and soon healed. The patient was discharged entirely free from all symptoms.

He has been working steadily for about two years as an engraver. He gained about 60 pounds (27.2 Kg.) in weight; the wound has remained solidly healed and he seems to be entirely well.

This case is of particular interest not only because it is a case of multiple abscesses of the lung successfully treated by cautery pneumectomy but also because there seemed to be undoubted evidence of cerebral embolism which cleared spontaneously.

CASE 3.—*Cautery Pneumectomy for Multiple Chronic Abscesses of the Lung with Bronchiectasis.*

T. G. G., a white woman, aged 23, in December, 1926, developed a cough and abundant foul expectoration which she believed were in some way connected with the extraction of a tooth in July, 1926. In March, 1927, she was operated on elsewhere for a right-sided empyema (?). Her sputum increased in amount following this operation. She was admitted to Barnes Hospital on March 26, 1927, and was operated on April 2 (fig. 3). The remaining portions of the ribs which had already been resected were removed for a distance of several inches and about 4 inches (10.16 cm.) of each of the two ribs immediately above. A small empyema cavity was found to communicate with the cavity already established and into this empyema cavity there opened three sinuses from different cavities of the lung, each of which discharged pus. Above this another large pocket which seemed to be mostly an empyema pocket was found. This large pocket contained about 50 cc. of foul smelling pus together with large masses of fibrin. The condition was therefore a multilocular abscess of the lung draining

into two different empyema cavities. The operation consisted in the removal of the roof of various cavities by the actual cautery, thus converting several small, improperly drained cavities into a single large one which could thereby be drained properly. The operation was terminated at this point.

On July 16, 1927, some remaining pus pockets in the lung were cauterized. The entire diseased area had now apparently been converted into a single large cavity. Recovery was rapid and the wound healed save for a small sinus which would not admit the tip of the finger. The patient was discharged from the hospital on August 20, and was readmitted on September 26, because the sinus had failed to close. She still had a slight cough and slight mucopurulent expectoration. On Jan. 30, 1928, a cautery was plunged into the lung along the old fistulous tract and a multilocular cavity which contained 30 cc. of foul smelling



Fig. 3.—The condition of bronchiectasis and multiple abscesses of the lung found in case 3 before cautery pneumectomy. The patient has now been completely well for a year and a half.

pus was entered. The roof of this cavity was removed with the cautery and it was tightly packed with gauze.

The postoperative course was uneventful. The patient is now shown to you, completely well. The wound is solidly healed and there are no symptoms.

Like case 2, we believe that in this case also the operation of cautery pneumectomy offered this patient the best chance of a complete recovery with at the same time the lowest risk. Simple drainage could not have been effectively carried out, collapse operations would have been likely to block whatever drainage already existed and thereby be dangerous, and ordinary lobectomy would have been both difficult and hazardous.

Unfortunately, in some cases after the operation of cautery pneumectomy a permanent bronchial fistula remains. The next case illustrates this condition. Ordinarily we do not attempt to close such a fistula until after at least two years have elapsed, because it often acts as a safety valve for residual infection of the lung.

CASE 4.—Cautery Pneumectomy for Subacute Abscess of the Lung with Fistula.

M. A., a white woman, aged 43, was admitted to Barnes Hospital on Aug. 30, 1922. Two months previously to admission she had her tonsils removed and following this operation developed signs and symptoms suggestive of abscess of the lung.

Physical and fluoroscopic examinations indicated a localized lesion in the right lung near the hilum. Pneumothorax treatment was attempted but was discontinued because of adhesions. A two-stage cautery pneumectomy was performed. The patient was discharged from the hospital on December 23, with a discharging sinus. Her condition improved until December 28, when she contracted a cold and cough and sputum returned. She developed severe pain in the side on which the operation had been performed.

She was readmitted to the hospital and on Jan. 18, 1923, further cauterization of the lung through the old incision was done. The patient was discharged from the hospital free from symptoms. A bronchial fistula which remained was partially closed by a plastic operation. Although she still has a bronchial fistula, she has been free from all symptoms for more than five years.

The following case illustrates not only an extensive cautery pneumectomy, but also the closure of several bronchial fistulas which remained. The result has been most gratifying. One interesting feature is that the boy was only 5 years old at the time of the cautery operation.

CASE 5.—Cautery Pneumectomy for Chronic Abscess of the Lung and Bronchiectasis.

D. B., a colored boy, now 11 years of age, was admitted to St. Louis Children's Hospital on Sept. 6, 1923, complaining of severe cough and copious foul expectoration. In August, 1922, he contracted a right-sided pneumonia. A thoracostomy for empyema was performed at the City Hospital in September, 1922. The cavity was drained for seven weeks and then apparently healed. In March, 1923, the patient had an attack of measles which was followed by a persistent fever. Shortly after this an abscess situated in the region of the right scapula was said to have ruptured into the lung and the patient began to be troubled with cough and foul expectoration.

On admission, physical signs combined with roentgen and fluoroscopic observations localized the lesion to the right lung. The lesion extended downward both anteriorly and posteriorly from the fourth rib.

On Sept. 8, 1923, with the patient under nitrous oxide anesthesia, a cautery pneumectomy was performed. The pleura was found to be adherent. The right lower lobe was indurated and nodular. Almost the entire lower lobe was burned out with the cautery. Six different abscess cavities were cauterized. The post-operative course was uneventful.

One month following operation the patient developed a bronchopneumonia which ran the usual course and from which he completely recovered. He was

discharged on December 23. The wound was entirely healed except for the presence of several bronchial fistulas. These were closed by an extensive plastic operation four years later. The patient is now entirely free from symptoms (fig. 4).

CASE 6.—*Cautery Pneumectomy for Chronic Abscess of the Lung and Bronchiectasis.*

E. J. H., a white man, aged 28, was first admitted to Barnes Hospital on Nov. 26, 1926, complaining of cough and mucopurulent expectoration. The onset of his illness apparently followed pneumonia at the age of 8 years. He also had another attack of right-sided pneumonia four months previous to his first admission.



Fig. 4.—External appearance of healed wound in case 5. After cautery pneumectomy, the boy had a large cavity with many bronchial fistulas. A plastic operation was performed in two stages, the wound is now solidly healed and the boy is free from symptoms. At the time of this photograph some of the scar tissue had not yet become pigmented.

From that time on his sputum was foul, occasionally blood-tinged, and he was also troubled by fever and occasional chills.

Physical examination suggested an abscess in the right lower lobe of his lung. A bronchoscopic examination performed by Dr. Arbuckle showed the right lower main bronchus to be constricted by what appeared to be a sort of web. This web was dilated and considerable pus escaped from the right lower lobe bronchus. Bronchoscopic treatment was continued at intervals. On March 7, 1927, a pneumothorax was attempted but proved unsuccessful because of pleural adhesions. Because of failure to improve under the aforementioned treatment a cautery pneumectomy was undertaken.

On March 9, 10 cm. of the seventh, eighth and ninth left ribs were resected. The lower lobe was found to be adherent, the upper lobe nonadherent. On March 16, the left lobe was entered by the actual cautery. About 250 cc. of thick foul pus was obtained. The patient was discharged after the operation much improved. Many bronchial fistulas were still present. Cough was practically negligible and the expectoration scanty.

A right phrenicectomy was performed on Feb. 6, 1929, in an attempt to diminish the size of the anatomic defect. The diameter of the wound appeared to be appreciably reduced following this procedure, although complete obliteration of the cavity will require further plastic operations. The patient is entirely free from symptoms.

BRONCHIECTASIS

We are of the opinion that all cases of chronic pulmonary suppuration are associated with some degree of bronchiectasis. In some cases the bronchiectasis is the more conspicuous part of the clinical and pathologic picture and in other cases the picture is chiefly that of chronic abscess of the lung. The next few cases which we are going to present will illustrate certain phases of bronchiectasis.

In our routine handling of cases of bronchiectasis we emphasize particularly the importance of the examination of the nasal sinuses in addition to the examination of the chest and of other parts of the body. There is no doubt in our minds that often the symptoms of bronchiectasis are made worse by chronic infection in the nasal sinuses. Conversely, it has been a frequent observation that after proper treatment of badly infected nasal sinuses the amount of purulent sputum is very greatly diminished. This result is often so gratifying that a patient's condition may be changed from an intolerable one into one of reasonable comfort merely by correcting chronic lesions of the nasal sinuses. Also it is needless to say, of course, that we feel that no examination in these cases is complete without the use of iodized oil. The method of using iodized oil, however, which we employ here is the very simple one devised by Dr. Singer which will be described separately at the close of this clinic. We also examine the sputum carefully not only for tubercle bacilli, but also for spirochetal organisms, because we think that in certain cases the use of arsphenamine and similar arsenic compounds is of some benefit. We, however, have never seen any startlingly beneficial results in bronchiectasis following the use of arsenical compounds even when the sputum contained many spirochetes. It is, of course, very necessary that the sputum be carefully examined for tubercle bacilli since bronchiectasis is a common result of chronic pulmonary tuberculosis, especially bronchiectasis in the upper lobes.

In regard to the treatment in those cases in which there are large dilated bronchi, like the fingers of a glove, in an atelectatic lobe which is the site of chronic suppurative pneumonia, we feel that no method that has yet been proposed is entirely satisfactory. After our examinations

have been completed we usually begin the treatment in such cases by comparatively simple devices. For instance, we like to put such patients on postural drainage for a few days, in order to insure them of fairly satisfactory drainage during that time and in order to relieve them of the fatigue which is sometimes incident to the repeated hard coughing which is necessary without the postural drainage. We sometimes use artificial pneumothorax when few or no adhesions are present and occasionally we have had very gratifying results. We do not feel that we can predict the presence of adhesions without introducing a needle into the pleural space. If good manometer readings are noted, air is introduced, and a therapeutic pneumothorax is maintained for several months if the collapse is satisfactory. Phrenicectomy has been of some value to us, especially if the diaphragm is mobile before the operation is performed, and particularly in cases of the lower lobe. We think that one of the explanations of the benefit from phrenicectomy is that a lower lobe may thereby be elevated and correspondingly the dilated bronchi may be brought into a more nearly horizontal position which thereby promotes better drainage. We do not think that the benefit from phrenicectomy is to be ascribed entirely to compression. The operation of phrenicectomy should not be undertaken lightly in our opinion in these cases because it sometimes interferes seriously with the expulsion of pus by coughing, and it occasionally results in the production of a severe suppurative pneumonia. Our experience with thoracoplasty in the treatment of chronic pyogenic bronchiectasis has not been so satisfactory as the reported results of others. In many cases we have used the operation of cautery pneumectomy, but we prefer to use this operation in the cases in which the predominant lesion is a chronic abscess of the lung, either single or multiple.

CASE 7.—Bilateral Bronchiectasis and Nasal Sinusitis Treated with Pneumothorax, Tonsillectomy and Surgical Drainage of Nasal Sinuses.

E. B., a boy, aged 11, was admitted to St. Louis Children's Hospital on March 11, 1924. In the summer of 1921, three years previous to his admission, he had an adenoidectomy. In the fall of that year he became ill with high fever and a cough which was associated with copious expectoration of mucopus. This illness lasted several weeks. From that time until admission, he had numerous similar attacks which lasted from two weeks to two months. The patient's mother said that frequently the boy coughed up as much as a pint of sputum in a day. Between attacks he would be entirely free from symptoms.

Physical, roentgen and fluoroscopic examinations, on admission, indicated a bilateral bronchiectasis, more marked on the right, although positive proof was lacking because this patient was observed before our use of iodized oil. Pneumothorax treatment of the right lung was started. The refills varied from 275 to 350 cc. of air. A good collapse was obtained. The patient was discharged on April 21, much improved both subjectively and objectively. Eight months later, the maxillary antrums were irrigated and tonsillectomy performed. Since then he has been free from symptoms.

This case illustrates a rather frequent combination of subacute nasal sinus infection with the symptoms of bronchiectasis. The sinuses in this case were treated by operation. The tonsils and adenoids were removed. The boy is now normal; he is gaining weight and is free from cough and sputum. Even in some cases of advanced bronchiectasis the amount of cough and sputum is greatly reduced after the establishment of effective drainage of chronically diseased nasal sinuses.

Occasionally, simple surgical measures produce excellent results. Phrenicectomy in addition to postural drainage is effective in a certain type of case. We have found that the elevation of the diaphragm sometimes changes the course of the bronchial tubes so that drainage by proper posture is very effective.

CASE 8.—Unilateral Bronchiectasis Treated with Phrenicectomy and Postural Drainage.

M. V. B., a white woman, aged 42, was admitted to Barnes Hospital on Feb. 8, 1928, complaining of cough, sputum, pain in the chest and afternoon fever. The onset of her symptoms dated back to 1925. At that time she had contracted pneumonia following a cesarean section which left her with a cough, copious expectoration and occasional hemoptysis. Rest in bed failed to clear up the condition, which was diagnosed pulmonary tuberculosis.

After admission to Barnes Hospital her sputum on repeated examinations was found negative for tubercle bacilli. Physical examination suggested a partial obstruction of the left lower lobe bronchus. A diagnostic bronchoscopy and injection of iodized oil revealed the presence of bronchiectasis of the left lower lobe. Postural drainage was started but was followed by only moderate improvement.

A left phrenicectomy was performed on February 23. The patient's symptoms became less pronounced, and gradually disappeared. She is now quite well.

This case illustrates the foregoing remarks. The patient had frequent hemorrhages, sputum and fever. She was in a tuberculosis sanatorium as a bed patient for two years without any definite improvement. Since phrenicectomy, her cough has ceased, she has gained weight and she has had no hemorrhages.

The patient in the following case was considered tuberculous for many years. Several months after the operation, he was able to do his work as a school janitor. He has had no recurrence of symptoms to this date.

CASE 9.—Cautery Pneumectomy for Abscess of the Lung and Bronchiectasis.

E. H., a white man, aged 40, apparently enjoyed good health until September, 1922, when he began to complain of loss of appetite and soreness all over his chest. A diagnosis of pulmonary tuberculosis was made, and he was given heliotherapy. It is to be noted that even on this occasion the patient had a productive cough and foul mucopurulent sputum. Some time later, a diagnosis of abscess of the lung was made, and he was admitted to Barnes Hospital.

The preoperative diagnosis was abscess of the left lower lobe and bronchiectasis. On July 30, 1923, 4 inches of the seventh and eighth left ribs were resected

subperiosteally. The lung was seen to glide back and forth with respiration through the unopened pleura, and for that reason the pleura was not opened but iodoform gauze was packed against it to produce adhesions. The left lower lobe felt firm and indurated. On August 6, the pleura was found to be greatly thickened. The cautery was then plunged into the indurated portion of the lung, and a cavity containing 10 cc. of thick pus was found. The roof of the abscess cavity was burned out with the cautery.

The postoperative course was uneventful. Cough and expectoration ceased after the operation and have not returned. The patient's wound healed completely.

PULMONARY TUBERCULOSIS

It has been our practice to treat all patients with unilateral pulmonary tuberculosis on the expectant plan for several months. If the patient does not improve sufficiently to warrant continuing this plan, pneumothorax treatment is instituted. This treatment is continued a sufficient length of time before phrenicectomy is resorted to followed by thoracoplasty.

We feel that patients should be in good general condition and if possible be "fever-free." Gain in weight is not sufficient evidence of good condition. A fixed mediastinum, particularly when it is drawn to the diseased side, is important. All patients should have pneumothorax if possible.

We have had some excellent recoveries after thoracoplasty but a few cases have not been benefited. We have had occasional deaths following operations from pneumonia in the opposite lung and occasionally massive collapse of the lung occurred. We are somewhat more radical in the extent of ribs removed than others. Our unsatisfactory results have occurred in cases in which we concluded that too small segments of ribs had been removed.

The following cases demonstrate the value of thoracoplasty in tuberculosis:

CASE 10.—*Unilateral Tuberculosis Treated with Phrenicectomy and Thoracoplasty.*

D. P., a man, aged 27, was admitted to Barnes Hospital on Sept. 27, 1927, with a diagnosis of pulmonary tuberculosis, referred by the Missouri State Sanatorium. The onset of his illness dated back to 1919 when he developed a dry, nonproductive cough which was shortly followed by pulmonary hemorrhage. Frequent attacks of hemoptysis had been his chief outstanding complaint. He worked at intervals until September, 1925. During this period hemoptysis was frequent. He received pneumothorax treatment from September, 1925, until September, 1927, at a tuberculosis hospital in Kansas City and at the Missouri State Sanatorium. On Oct. 13, 1927, a thoracotomy was performed and several adhesions of the upper lobe were cut. Pneumothorax treatment was then continued. The pleural effusion in the left pleural cavity which had developed after the thoracotomy gradually resorbed. The patient was discharged on December 12.

Since pneumolysis the patient has been entirely free from cough, and he also has had no hemoptysis since pneumothorax treatment was started. He was read-

mitted to the hospital on Sept. 18, 1928, complaining of weakness, heart burn and tremors. A large left-sided pneumothorax was still present. The aforementioned complaints were apparently due to the pneumothorax treatment. If, however, the patient was allowed to miss a refill he would be troubled with pains in the chest, expectoration and general malaise. On September 20, left phrenicectomy was performed. Three weeks later thoracoplasty was started and was completed in two stages with removal of portions of first to eleventh ribs, inclusive. The patient now has a feeling of well-being and is gaining in strength and weight. His appetite has returned. There is no cough or fever.

CASE 11.—*Unilateral Tuberculosis Treated with Thoracoplasty.*

A. S. W., a white woman, aged 38, was admitted to Barnes Hospital on Dec. 7, 1925, complaining of chronic cough of seven years' duration, occasional slight hemorrhage from the lung, and fever. Three of her brothers had died from pulmonary tuberculosis. During the six months previous to admission, she had lost 16 pounds (7.3 Kg.) in weight.

Physical examination showed râles over the apex of the left lung and diminished breath sounds and whispered sounds over the entire left side of the chest. The physical signs suggested a cavity in the upper lobe of the left lung. The leukocyte count was 21,650. The sputum contained many acid-fast bacilli, and the temperature varied between 37.5 and 39 C. (99.5 to 102.2 F.). The patient had two hemorrhages after her admission to the hospital. Repeated pneumothoraces were done, from 200 to 300 cc. of air was introduced on each occasion and a good collapse of the lower lobe was obtained, but the cavity in the left upper lobe remained uncollapsed because of adhesions. A thoracoplasty in two stages was then performed. The temperature remained normal after operation, and there was an immediate reduction in the cough and expectoration. In a short time the patient was free from symptoms, and she has remained so since.

This patient had fever continuously for two years before the thoracoplasty. Almost immediately after the operation her temperature became normal, and it has remained so ever since.

CASE 12.—*Unilateral Tuberculosis Treated with Thoracoplasty.*

H. E. R., a white woman, aged 41, was admitted to Barnes Hospital on Sept. 24, 1926. She came from the Missouri State Sanatorium with a diagnosis of pulmonary tuberculosis. Her symptoms dated from the birth of her baby three years previous to her admission. Shortly after the birth of the child she developed a cough and started to lose weight. Four months after the onset of these symptoms, she developed a high fever. While at the sanatorium she regained her lost weight but her cough and elevation of temperature persisted.

On admission, physical signs, fluoroscopy and roentgenograms revealed a tuberculous process in the left lung. The right lung showed no evidence of active tuberculosis. The patient's sputum was found to contain tubercle bacilli. On September 28, a first stage thoracoplasty was done. Two weeks later the second stage operation was performed. The postoperative course was uneventful. A good collapse was obtained. The patient was discharged on December 21, greatly improved. Her cough and expectoration were negligible.

One of the conditions in which the most gratifying results may be obtained by extrapleural thoracoplasty is tuberculous empyema, a condi-

tion which formerly was almost uniformly fatal. Some cases of tuberculous empyema, however, tax the utmost ingenuity of the surgeon. The following case is an example of such.

CASE 13.—*Chronic Tuberculous Empyema Treated with Thoracoplasty.*

R. L. P., a man, aged 21, in November, 1918, had a severe attack of influenza. Three weeks later he was operated on at another hospital for a right-sided empyema and portions of two ribs were removed. On February 28, he was taken home on a stretcher and remained in bed until May 1, 1919. The tube came out in July, 1919, but a sinus remained. In November, 1919, another rib was resected and another tube was put in. This tube remained in until the latter part of 1920. His empyema cavity was then irrigated with some antiseptic solution and apparently closed. On Feb. 1, 1921, the wound began to discharge once more and portions of three ribs were resected. The patient was again operated on in July, 1921.

He was first admitted to Barnes Hospital on April 27, 1922. His wound was still draining and tube was still in place. Operation was performed on May 10. Several sinuses were found beneath the skin and also beneath the muscles and the ribs. One of these communicated directly with a sinus high in the neck. The parietal pleura over the empyema cavity which had a capacity of 100 cc. was markedly thickened. The cavity extended upward and posteriorly and had a very narrow sinus opening into its apex. Large drain tubes containing Carrell tubes were introduced into the various sinuses to try to obliterate the empyema cavity by conservative measures before undertaking more radical procedures. On June 3, 1922, it was found that all sinuses communicated. They were laid open widely. In order to do this it was necessary to sever some of the fibers of the trapezius and rhomboid muscles, as some of the sinuses were chiefly between these muscles and the wall of the chest. The granulation tissue which was excised for microscopic examination showed miliary tubercles. On August 15, the entire cavity apparently measured only 25 cc. On Sept. 11, 1923, it was found that a ring of bone had formed around the entrance to the main drainage tract and was perhaps partly responsible for the failure of the empyema cavity to heal. It was completely removed and it was then observed that only a long sinus tract which would hold about 50 cc. remained. A flap of the pectoralis major muscle was dropped into the tract, and a little pressure with an ordinary sea sponge was made on the skin flap.

The patient was discharged much improved. His sinus discharged but little. He had gained in strength and weight. He reentered the hospital on Nov. 9, 1927, after an interval of four years, complaining of some discharge from two sinuses in the right axillary region. On November 11, a portion of newly formed bone over the two discharging sinuses was removed, and it was then found that the cavity could be completely obliterated by pressure. The patient was discharged on November 23. One small sinus still remains.

This patient had several operations elsewhere. It was found necessary to do a complete thoracoplasty and to open several sinuses before any good results were obtained. He has been working as a clerk in a railroad office for several years in spite of a small discharging sinus.

CASE 14.—*Unilateral Tuberculosis and Tuberculous Empyema Treated with Pneumolysis, Phrenicectomy and Extrapleural Thoracoplasty.*

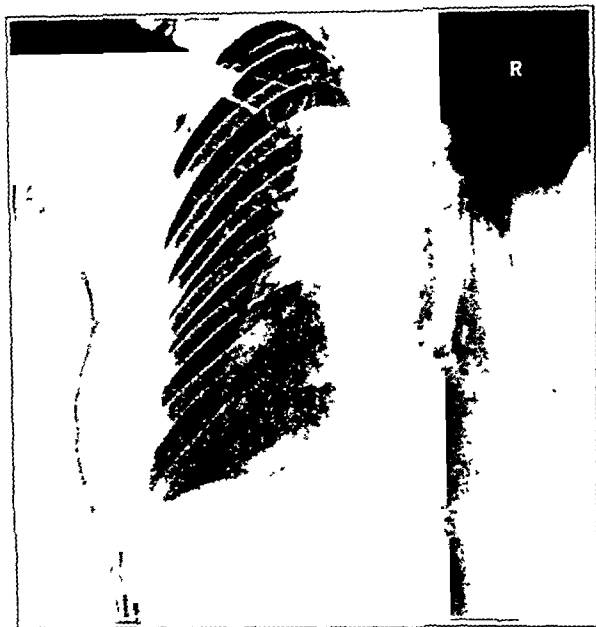


Fig 5.—Final result in case 14, a case of unilateral tuberculosis and tuberculous empyema.



Fig. 6.—Same patient as in figure 5 with wound solidly healed.

A woman, aged 19, was admitted to Barnes Hospital on Jan. 24, 1928. For three and one-half years previous to admission, she had chronic productive cough, slight elevation in temperature in the afternoons and loss of weight. For three years she was a patient at the state sanatorium at Mount Vernon, Mo., during which time she received pneumothorax treatment with marked improvement. The treatment was therefore discontinued and the lung allowed to reexpand. After four months she had a recurrence of all her symptoms, and pneumothorax treatment was again started.

Physical examination of the patient on her admission to Barnes Hospital revealed a tuberculous process in the right upper and middle lobes. Complete collapse by artificial pneumothorax was found to be impossible because of adhesions. On Jan. 31, 1928, with the patient under gas anesthesia, a right pneumolysis was performed and one adhesion was severed by the cautery. At the time of the pneumolysis several tubercles were found on the pleura. Following this operation, good collapse was obtained. The patient then developed clear fluid in her right pleural cavity. Repeated aspirations were necessary, and large amounts of fluid were withdrawn. Further attempts at pneumothorax proved unsuccessful. A right phrenicectomy was done on April 3. A bulging of the pneumolysis incision then developed. This was found to be a tuberculous empyema necessitatis, which was drained.

A right thoracoplasty was later done in two stages. The postoperative course was satisfactory. The patient was discharged on October 18, with the tuberculous process completely healed. All symptoms present on admission had been arrested (figs. 5 and 6).

CASE 15.—*Chronic Nontuberculous Empyema Treated with Thoracoplasty.*

J. C. S., a white man, aged 39, was first admitted to Barnes Hospital on April 5, 1920. His chief complaints on admission were those referable to a chronic left-sided empyema which had resulted from a bullet wound in 1908. The bullet had been removed but the wound continued to drain. Two years later (1910), portions of two ribs were resected to permit of freer drainage. After this procedure, the patient improved sufficiently to return to work. His wound did not heal entirely, but there was little discharge for the next two years. In 1912, the discharge became more profuse, and portions of more ribs were resected. The wound healed, except for one small sinus, and he was free from disturbing symptoms from 1912 to 1920.

Two months previous to admission to Barnes Hospital, he began to have pains in the left side of the chest and arm, which became so severe that he was unable to use his arm. On April 9, 1920, an incision was made just superior to the tunnel-like sinus. The newly formed ribs were found to be enormously thickened and fused. This large plaque of bone was removed and a shallow cavity uncovered which extended almost to the apex of the lung. A muscle flap was turned into the cavity after the lower 2 inches (5 cm.) of the scapula had been resected. The patient was discharged from the hospital on June 23, 1920. The empyema cavity and sinus had been obliterated, and the wound was entirely healed.

The patient was again admitted to Barnes Hospital on Aug. 18, 1920, for an osteomyelitis of the radius and ulna of the left arm. On Aug. 29, 1921, he was admitted for incision and drainage of a subperiosteal abscess of the left humerus, and on Jan. 19, 1927, for chronic osteomyelitis of the right tibia.

This patient's last admission was on Dec. 8, 1928, because of severe pain under the left shoulder blade. A slight discharge from the old operative wound on the right leg was still to be noted. Breath sounds over the apex of the left lung

posteriorly were diminished. The muscles over this area were tense and tender. On December 24, an incision was made over this tender area and about 200 cc. of thick, odorless pus which contained a pure culture of staphylococci was removed. No opening into the pleura could be demonstrated. The possibility of a subperiosteal abscess of osteomyelitis of a rib could not be excluded. The patient was discharged from the hospital on Jan. 19, 1929. His wound is entirely healed, and he is now free from all symptoms referable to his chest.

TUMORS OF THE PLEURA AND LUNG

Tumors of the pleura and lung represent interesting problems in chest surgery. The malignant type of tumors have been particularly



Fig. 7.—Myxoma of mediastinal pleura removed from case 16. The scale is in centimeters.

so. We feel that patients with such conditions, if seen early, might be benefited by surgical measures, but they rarely present themselves for diagnosis and treatment. One of our patients who had a small bronchial carcinoma which was removed bronchoscopically is still free from any evidence of recurrence a year later. Many others were treated by cautery, the roentgen rays and radium, but all cases ended fatally.

CASE 16.—*Myxoma of Pleura, Surgical Removal.*

F. N., a man, aged 54, was admitted to Barnes Hospital on May 25, 1923, complaining of a lump in the right breast. Physical examination revealed a spherical tumor situated in the region of the third and fourth ribs on the right side. There was no evidence of any pleural effusion or of any compression of

any of the large blood vessels. The tumor was firmly attached to the wall of the chest.

On May 28, 1923, operation was performed. The tumor was seen to be growing between the third and fourth ribs, which showed marked spreading as a result of pressure. The intercostal muscles were also thinned out. The tumor extended under the sternum, from which it could be easily separated. It apparently arose from the mediastinal pleura. A microscopic section showed typical myxomatous tissue (fig. 7).

The patient was discharged on June 9, 1923. He reported for observation on September 12, and then said that he was quite well and had been working for three months. At the present time he is perfectly well.

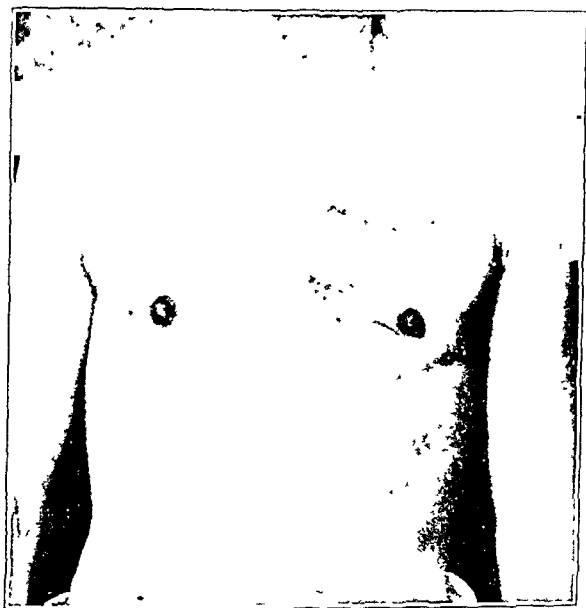


Fig. 8.—Scar in case 17 following cardiolysis for chronic mediastinal pericarditis.

CARDIOLYSIS

CASE 17.—*Cardiolysis for Chronic Mediastinal Pericarditis.*

We present this case not only because of an excellent result obtained but also because we feel that more interest in this type of case should be aroused than at present exists. The patient was referred to us by Dr. Elsworth Smith. He was admitted to the hospital in January, 1923, because of evidence of cardiac decompensation which had been present for six weeks. There had been no improvement after digitalis therapy. Atypical signs and features of chronic mediastinopericarditis were found on examination, and on May 2, 1923, with the patient under local anesthesia, the third, fourth and fifth ribs on the left side were resected from the border of the sternum to a line well out beyond the heart. This resection included both ribs and costal cartilages. Some of the sternum was also removed with a rongeur. The periosteum and perichondrium of the ribs were carefully stripped from the pleura so that there would be no regeneration

of new bone or new cartilage. The pleura was not opened. His recovery from the operation was prompt and he has been at work now for more than five years in a clerical position which requires him to work for ten hours a day. He has had no return of cardiac decompensation since the operation. This operation should be performed much more often than it is, because there are many more persons seriously handicapped by chronic mediastinal pericarditis than is commonly realized (fig. 8).

RESULTS OF CAUTERY PNEUMECTOMY IN CHRONIC PULMONARY SUPPURATION

We thought that it would be of interest to report to the organization at this time the results of the cases of chronic pulmonary suppuration treated by the operation of cauterization pneumectomy. It should be understood that this operation is reserved for only the most refractory cases. We find, moreover, that it is of greater value and probably less dangerous in those cases in which the predominating features of the picture

Data on Cases of Chronic Pulmonary Suppuration Treated with Cautery Pneumectomy

Number of cases	54	
Definitely improved	36 (66.7%)	
Moderately improved	2 (3.6%)	
Slightly improved	3 (5.6%)	
Not improved	7 (12.8%)	
Dead (operative mortality)	6 (11%)	
Late Results		
Number of cases	54	
Number of patients still alive	36 (66.7%)	All patients at work
Definitely improved	34 (63%)	
Moderately improved	1 (1.6%)	
Slightly improved	0	
Not improved	1 (1.6%)	
Operative deaths	6 (11%)	
Late deaths, not directly due to operation	12 (22%)	
Bronchial fistula still present	17 (47%)	

are of chronic abscess of the lung rather than of cylindric bronchiectasis. The statistics in the accompanying table do not include cases accompanied by carcinoma of the lung.

In the table we have divided the deaths into those which were directly ascribable to the operation and those which occurred late and were due to causes not directly ascribable to the operation. It is, of course, somewhat difficult to state with certainty that some of these late deaths were not caused by the operation, but since they include deaths which occurred at variable times from two months to two years after the operation of cauterization pneumectomy, it was felt that they should not be ascribed to the operation itself.

Of the twelve cases in which death occurred late after the operation, one was due to an acute enteritis which seemed to be entirely independent of either the operation or the original suppurative pulmonary condition. Another one was reported to us as a sudden death at home, the cause of which could not be ascertained. A third was due to pulmonary tuberculosis in a case in which the patient's original condition was a tubercu-

lous abscess which had been treated by cauterization and pneumectomy. A fourth patient died from bronchopneumonia which may have been due to residual infection in the lung. Two patients died more than a year later from brain complications; in one case an abscess of the brain and in the other meningitis. In these last two cases, the fatal lesions were due undoubtedly to the fact that some of the original infection in the lung still remained. In two patients, a generalized infection of the blood stream was present; in one instance it was associated with diabetes. It is probable the operation on these two patients should not have been undertaken. Two other patients died more than a year after the cauterization and pneumectomy as a result of operations to close the bronchial fistulas. In one of these cases death occurred suddenly, presumably due to air embolism, and in the other one the patient died as a result of a generalized infection presumably due to contamination of the wound by the pus from the bronchial fistulas. In both of these cases the patients were free from symptoms and died merely because they desired to have the bronchial fistulas closed. In two other cases death occurred from hemorrhage from bronchial fistulas. Both of these deaths occurred several months after the operation of cauterization and pneumectomy.

3. BRONCHOGRAPHY *

JACOB J. SINGER, M.D.

ST. LOUIS

We who work in the chest service of Barnes Hospital agree with others who regard bronchography as a method which has revolutionized the diagnosis of pulmonary conditions. Since the introduction of iodized oil 40 per cent, as suggested by Sicard and Forestier, we have been able to perform lung mapping without any danger to the patient and with most gratifying results in diagnosis.

There are seven methods of introducing iodized oil:

(1) Through a trocar needle, resembling a tracheotomy tube, into the trachea, under sterile precautions.

(2) Under direct laryngoscopic examination with the patient lying on the back, with the head extended over the table.

(3) Through the bronchoscope introduced directly into the lung.

(4) Through a tracheal catheter introduced under indirect illumination of the larynx.

(5) Through the passage of a specially constructed intubation tube.

(6) Passive method of aspiration. After complete anesthesia of tonsillar pillars and trachea, the patient is given the oil by mouth and instructed to aspirate it.

(7) By the injection into the pharynx of 20 cc. of oil while the patient pulls out his tongue as far as possible. The patient should be trained to take many successive deep breaths following the injection of the oil. This method which we proposed in 1925 is the one which we most commonly use.

The iodized oils used were lipiodol (Lafay), which contains 40 per cent of iodine by weight combined with poppy seed oil; and iodipin, which contains 40 per cent by weight combined with sesame oil. Iodipin can be obtained in either 10 or 40 per cent compounds. It is possible that other oils can be used, but the two mentioned are the ones we use in our work.

In these two products the iodine is so firmly combined with the oil that the iodine reaction cannot be obtained in patients who are expectorating sputum combined with the oil. Iodized oil is not rapidly broken down in the lungs but may be in the gastro-intestinal tract, when it is swallowed or when through accident the oil is introduced into the esophagus. Iodism may thus result.

The choice of the seven methods of technic in use usually varies with the experience of those interested in the methods. Laryngologists prefer the bronchoscope; pediatricians, the tracheal trocar. Medical men and

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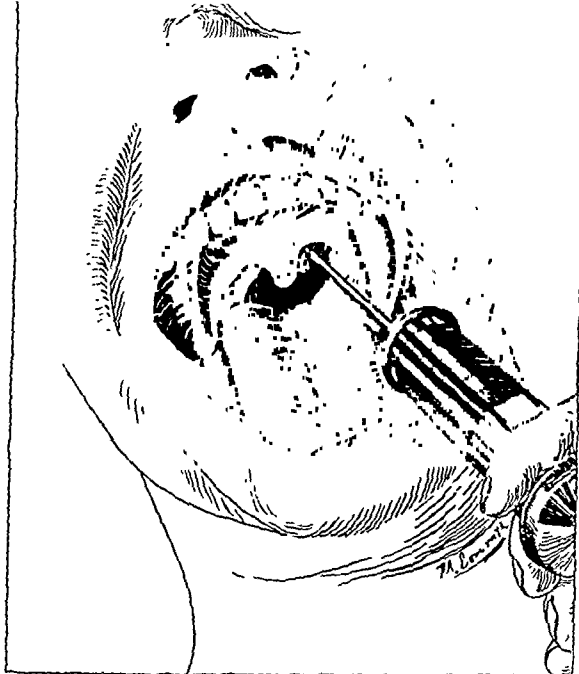


Fig. 1.—Method of introducing the iodized oil. The patient faces a good light and is told to open his mouth as widely as possible; his tongue is grasped with a piece of gauze and is pulled out as far as possible. Iodized oil which has previously been warmed in a syringe is slowly injected into the posterior pharynx through a straight cannula while the patient breathes deeply. The patient is urged not to swallow or cough during the injection. The use of a local anesthetic is seldom necessary.

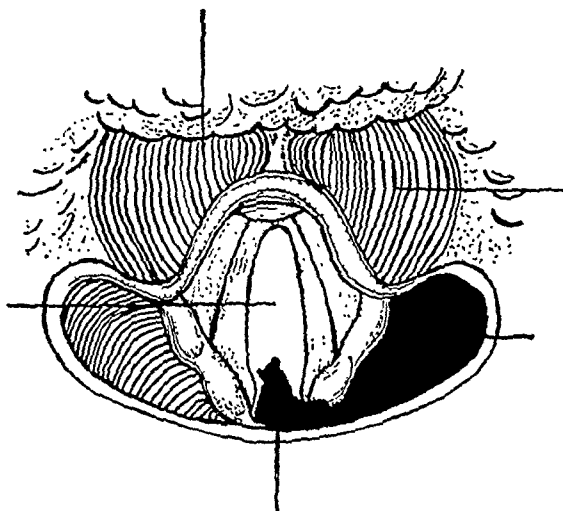


Fig. 2.—Iodized oil, introduced by the method illustrated in figure 1, collects in the interarytenoid fossae. It then trickles between the vocal cords during the phases of respiration and is thus aspirated into the bronchial tree.

roentgenologists prefer the intratracheal injection through the mouth. Irrespective of the method used, approximately from 20 to 40 cc. of the oil must be instilled to produce suitable roentgenograms.

The value of bronchography lies in the definite mapping out of lung structure, either normal or altered by pathologic conditions. It requires considerable experience to be able to interpret these shadows, especially with so dense or so opaque a substance. In view of the fact that the lung fields may extend in an anterior and a posterior direction from 6 to 12 inches (15.2 to 30.4 cm.), one can readily understand how superimposing shadows will complicate the roentgenogram, but the true interpretation will be made in conjunction with the physical signs and history. Many dense shadows in the roentgenogram may be tumor masses, collapsed lung tissue or cavities filled with secretion. The opacity of the iodized oil when introduced into the lungs of these patients will often give startling pictures of pathologic conditions that were not suspected.

The oil can be used in fistulous tracts to map out chronic empyema cavities and also bronchial fistulas, and when introduced in this way it rarely excites a cough. This substance has helped to show abscessed cavities that were connected with the empyema cavities through a bronchial fistula.

In pneumothorax cases, and especially in bronchiectatic cases, iodized oil shows well whether or not the bronchi are collapsed.

Jacobaeus, in a recent article, described how the iodized oil in pneumothorax cases has shown that bronchial tubes were seen in adhesions extending to the wall of the chest. One can easily see how it could be possible to sever lung tissue with the cautery in Jacobaeus' method of pneumolysis and produce an empyema and probably death.

To summarize the value of bronchography, it is of great benefit, in combination with careful physical examination, to those who have had considerable experience with suppurative conditions of the lung. It should not be used when simpler methods suffice for the diagnosis. It shows excellently the bronchial tree with abnormalities present, and when properly used it is harmless.

The first method is recommended for children, the fourth and seventh methods for adults, and the second and third methods when bronchoscopy is performed for other purposes. The seventh method should be tried in adults before attempting the more complicated ones. If successful, then the fourth is the method of choice.

Recently, Iglaue devised an intubation tube which prevents regurgitation of the oil. While this method has much to commend it, one should use means with as little instrumentation as possible to obtain the desired roentgenogram.

DEMONSTRATIONS OF EXPERIMENTAL WORK IN THE WASHINGTON UNIVERSITY SCHOOL OF MEDICINE

1. CALIBER CHANGES IN THE BRONCHI IN NORMAL RESPIRATION *

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ST. LOUIS

The use of iodized oil 40 per cent has permitted the outlining of the bronchial tree in the living subject with great accuracy and detail. This suggested it as a possible agent in determining the caliber changes believed to occur in the bronchi in normal respiration.

EXPERIMENTS

Observations were carried out on living subjects—one cat, two dogs and five human beings. The animals were anesthetized with ethyl carbamate (urethane), and the oil was administered by tracheal puncture. In man, where no anesthetic was required, the films were taken in the course of diagnostic procedures. After injection of the oil, x-ray films were taken during the actual process of breathing, and in man also while holding the breath at the end of inspiration and at the end of expiration. The respiratory movements were recorded by a pneumograph held around the chest by a tape and attached to a tambour. The moment of the time of exposure of the film was signalled on the record. To record accurately the time of exposure with reference to the particular phase of respiration it is well to have the kymographic marking key and the x-ray circuit operated by the same switch, but it was not possible to arrange this in these experiments. All roentgenograms were taken at a constant distance, 3 feet (91.44 cm.), and the exposures made short to avoid motion in the pictures.

Results showed that the bronchi and bronchioles are widest at the end of full inspiration and narrowest at the end of full expiration. In quiet breathing the changes in caliber are slight. In some of the long bronchi, particularly in those to the lower lobe, there is an actual narrowing during the first part of inspiration. While these observations were puzzling at first, it was seen that they could be explained on the

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* This report is in part an abstract of data presented in a paper, "A Method for the Demonstration of Calibre Changes in the Bronchi in Normal Respiration," published in *The Journal of Clinical Investigation* (4:459 [Oct.] 1927).

basis of passive changes. The roentgenograms showed that the bronchi, especially the ones to the lower lobe, lengthened considerably during respiration. Passive mechanical changes in caliber would therefore be the resultant of linear and radial traction. The linear changes would be greatest at the beginning of inspiration, at the time of the descent of the diaphragm, especially in respect to the lower lobes. Radial traction would be greatest at the end of inspiration on elevation of the ribs, when the anteroposterior and lateral diameters of the lungs are at a maximum. During quiet respiratory movements the tendency to widen during inspiration due to radial traction might almost be equaled throughout the greater portion of the lungs by the tendency to narrow due to linear traction.

To study the passive changes which might occur in the bronchi during inflation and deflation of the lungs, experiments were performed on two cats after death. The recently killed animal was placed in a large rigid cardboard paper cylinder so fitted that exhaustion of the air within the cylinder by a water suction pump was possible. A tracheal cannula, firmly tied in, opened to the atmosphere through a rubber stopper in the lid of the cylinder. The iodized oil was administered through the cannula. Roentgenograms were taken with the cat's lungs inflated and deflated by negative pressure to varying degrees. A waxed paper cylinder was used because it interfered with the passage of the x-rays less than glass.

The results proved that the longitudinal and radial changes demonstrated in the roentgenograms of the living lung could be paralleled in the dead lung when they were entirely passive. The sequence of passive changes was a shortening and narrowing of the bronchi with deflation; an elongation and possible narrowing with partial inflation and a widening with more extensive inflation.

The presence or absence of active influences in the respiration of the living subject was not determinable from the evidence of this investigation. Numerous researches have shown that the caliber of the bronchi is under nervous control. Even if there is no active participation on the part of the bronchial musculature in ordinary respiration, it would still exert its influence as an elastic structure the degree of stretching of which would vary with the degree of vagus and sympathetic tone.

Information having a bearing on the study of the nervous mechanism of the bronchi has been secured through an analysis of the action potential of the sympathetic and vagus nerves of the turtle. It has been found¹ that the action potential of the cervical sympathetic trunk

1. Heinbecker, Peter; and Bishop, George H.: *Proc. Soc. Exper. Biol. & Med.* 26:645, 1929.

is in general composed of two wave complexes, but that in certain of such nerves there are three. For the purposes of identification, these are named the *A*, *B* and *C* groups. When present, the *A* group has a threshold, a conduction rate and an absolutely refractory period time similar to the alpha, beta, gamma and delta groups of the frog sciatic as described by Erlanger and Gasser. The *B* and *C* groups have a threshold, conduction rate, chronaxia and absolutely refractory period time which differentiates them entirely from the *A* group. The threshold is higher, the conduction rate is less and the chronaxia and absolutely refractory time are approximately from five to ten times that of the *A* group. Microscopic sections indicate that the *A* group potential, when present, arises from the largest relatively thinly myelinated fibers in these nerves. The *C* group arises essentially from the unmyelinated fibers and the *B* group essentially from the small thinly myelinated fibers always associated closely with the unmyelinated nerve fibers.

The vagus nerve has an action potential similar in form to that of the sympathetic with the *A*, *B* and *C* potential groups. The properties of the potential groups are also the same as those of the sympathetic nerve.

The analysis of the form and properties of the action potentials of these nerves affords a basis for further work in the identification of the fiber groups in similar nerves responsible for functional changes occurring in the musculature of the bronchi in animals.

2. CHANGES IN THE SHAPE AND SIZE OF THE TRACHEOBRONCHIAL TREE FOLLOWING STIMULATION OF THE VAGO-SYMPATHETIC NERVE *

BYRON F. FRANCIS, M.D.
ST. LOUIS

Changes in the caliber of the bronchi in response to vagus stimulation have been observed by many. As long ago as 1842, Langet¹ directly observed constriction of the bronchi of the horse when the peripheral end of a cut vagus nerve was stimulated. Dixon and Brodie,² in 1903 and 1904, studied the effects of nerve stimulation by recording changes in intratracheal pressure and changes in the volume of a lobe of the lung which had been placed in an oncometer. The method was modified somewhat and used by Weber³ in 1914, and by Braeucker⁴ in 1925 and 1927, in making further studies. The results of the investigations of these and many others have been overwhelming proof that the caliber of the bronchi may be changed by impulses traveling through the vagus nerve. An admirable review of the entire subject has been presented by Macklin in a recent issue of the *Physiological Reviews*.⁵

However, a study of the changes in size and shape of the bronchi which take place within the intact chest as a result of nerve stimulation, and of how the respiratory movements might modify these changes has not been made. It is my purpose to record a study of these changes. The method used is similar to the one employed by Heinbecker⁶ in demonstrating changes in the size of the bronchi during normal respira-

* From the Chest Service of Barnes Hospital and the Department of Medicine, Washington University School of Medicine.

1. Langet: Recherches expérimentales sur la nature des mouvements intrinsèques du poulmon et sur une nouvelle cause d'emphysème pulmonaire, *Compt. rend. Acad. d. sc.* **15**:500, 1842.

2. Dixon, W. E., and Brodie, F. G.: The Bronchial Muscles, Their Innervation and the Action of Drugs upon Them, *J. Physiol.* **29**:97, 1903.

3. Weber, E.: Ueber Experimentelles Asthma und die Innervation der Bronchialmuskeln, *Arch. f. Physiol.* **142**:63 1914.

4. Braeucker, W.: Die Experimentelle Erzeugung des Bronchialasthmas und seine operative Beseitigung, *Arch. f. klin. Chir.* **139**:1, 1925; *ibid.* **137**:463, 1925. Braeucker, W., and Kummell, H.: Ueber die "reine" Vaguswirkung an den Bronchien, *Pflüger's Arch. f. Physiol.* **218**:301, 1927.

5. Macklin, Charles Clifford: The Musculature of the Bronchi and Lungs, *Physiol. Rev.* **9**:1 (Jan.) 1929.

6. Heinbecker, Peter: Method for Demonstration of Calibre Changes in Bronchi During Respiration, *J. Clin. Investigation* **4**:450 (Oct.) 1927.

tion. It is essentially the recording roentgenologically of the tracheobronchial tree after injections of a substance opaque to the roentgen ray have been made. By this means changes in the outline of the trachea and bronchi may be noted by comparison of the films that have been taken during various steps in the experiment.

EXPERIMENTS

Dogs and cats were used. The animals were anesthetized by sodium barbital injected intraperitoneally. Dry bismuth subcarbonate powder was blown into the tracheobronchial tree. This was found to be more satisfactory than iodized oil, because it coated the walls better and tended to remain as it was originally distributed, whereas the iodized oil soon flowed out of the upper bronchi into the

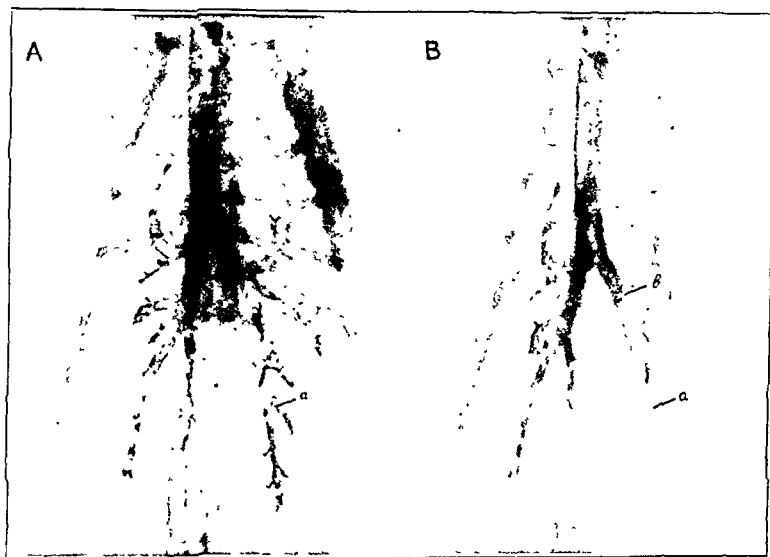


Fig. 1 (cat).—Both vagosympathetic nerves were cut to slow and deepen respirations. *A* was taken at height of inspiration; *B*, at end of expiration. The small letters *a* and *b* in this and in figure 4 indicate comparable regions of the tracheobronchial tree.

lower bronchi or into the alveoli, drowning portions of the lung. The vagosympathetic nerve was isolated in the neck, and stimulation was effected by a faradic current.

X-ray plates of the chest of the animal were taken with the tube at a constant distance from the plate; in this series the distance was 26 inches (65.96 cm.). To determine the time and duration of the exposure in relation to the respiratory cycle, records of the respirations and exposure were made simultaneously on a kymographion. Closing of the switch of the x-ray machine also closed the key of the marker on the drum. A record was similarly made of the time and duration of the stimulation of the nerve.

In figure 1, *A* was taken in inspiration. That this is so is noted by the increase in the width of the chest and the depth of the diaphragm. It

is easily seen that the entire bronchial tree, including the trachea as well as the bronchi, is longer and wider. Actual measurements of a portion of the left bronchus between the two marks are: on inspiration an average width is 3.75 mm., the length, 37 mm. For the purpose of comparison, if I may be permitted to compute the probable capacity of the tubes from these data, it is seen that the capacity of this section of tube is about 1,634 c.mm. In expiration, the length of this tube has become 33 and the width 3 mm., giving a capacity of about 933 c.mm.

The capacity in inspiration is therefore 1.75 times that in expiration. If this is an indication of the extent of changes throughout the bronchial tree, as it seems to be, the dead space of the lungs is far from a fixed quantity. This fact has been pointed out many times before. Changes in the size of the bronchi during the respiratory cycle were surmised by Keith⁷ and demonstrated by Macklin⁸ and Heinbecker.⁹ Ballon and Ballon⁵ have shown changes in the size of the bronchi which had been filled with iodized oil by making an exposure during inspiration and during expiration on the same plate.

In figure 2, it is to be noted that the size of the chest is the same in *A* and *B*. By actual measurement on the film the chest in *B* is 2 mm. narrower than that in *A* at a level which is just below the bifurcation of the trachea, but otherwise there is no change. It will be noted, however, that there is a general narrowing of about 1 mm. of the right bronchus. The trachea is narrower also. The left bronchus is slightly narrower. That the two plates were taken in the same phase of respiration is further shown by the record. In figure 3, it is seen that the control plate, figure 2 *A*, was made just at the beginning of inspiration (2). Figure 2 *B* was taken at 5, which is at about the same point in the respiratory cycle as 2, and about eleven seconds after stimulation of the peripheral end of the cut right vagosympathetic nerve began. The beginning of stimulation is indicated at 4. More marked changes in size and shape of the bronchi are shown by stimulation of the uncut vagus nerves.

The most marked changes in size and shape of the tracheobronchial tree occurred when the intact vagi were stimulated. By comparing figure 4 *A* with figure 4 *B*, a marked difference is seen.

In figure 4, both exposures were made with the animal in an oblique position. The chest of the animal is narrower in *A* than in *B*, but the

7. Keith, A., in Hill, L.: *The Mechanism of Respiration in Man in Further Advances in Physiology*, London, E. Arnold, 1909.

8. Macklin, C. C.: *X-Ray Studies on Bronchial Movements*, *Am. J. Anat.* 35:303, 1925.

9. Ballon, D. H., and Ballon, H. C.: *Pneumonography with Iodized Oil, 40 Per Cent, by Bronchoscopic Method: The Bronchial Tree, with Observations Made from One Hundred Injections*, *Arch. Surg.* 14:184 (Jan.) 1927.

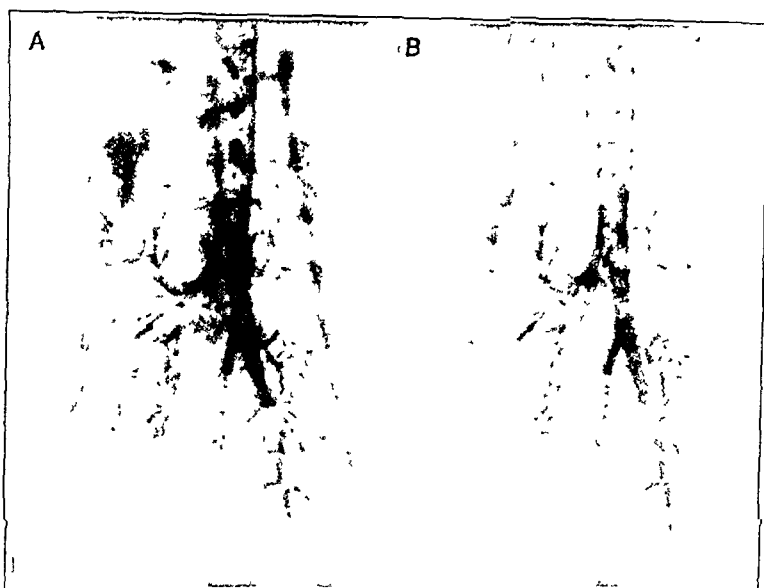


Fig. 2 (cat) —Both vagi were cut. *A* was taken before stimulation; *B*, during stimulation of the peripheral end of the right cut vagus. Both exposures were made at the same phase of the respiratory cycle. See figure 3.

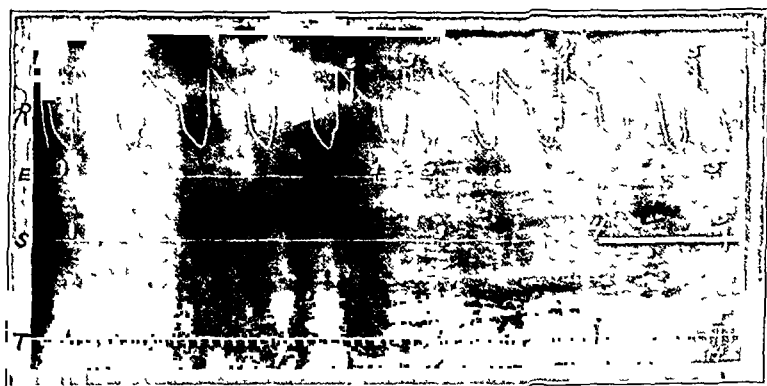


Fig 3.—Simultaneous record of respirations, time of exposure, time and duration of stimulation made. *R* indicates the respiratory tracing, upstroke is expiration, downstroke is inspiration; *E*, exposure; *S*, stimulation; *T*, time in seconds. Figure 2 *A* was taken at 2; and figure 2 *B* at 5.

diaphragm is at the same level in each. Measurements of the left bronchus give some significant results. Between the two marks the distance is 30 mm. in each but the diameter in *A* is 1.75 and in *B* it is 4 mm. A calculation of the capacity gives 72.159 for *A* and 376.99 c.mm. for *B*, a change of more than five times. Only a slight edema of the mucous membrane of a bronchus so constricted would completely occlude its lumen. The localized constriction of the right bronchus with the dilated region beyond the narrow portion gives one the impression of a peristaltic-like wave in process.

It does not seem likely that this change in the bronchi is a passive one due entirely to changes in capacity of the chest from a disturbance



Fig. 4 (cat).—Oblique position, *A* was taken during stimulation of both uncut vagosympathetic nerves in the neck; *B*, two minutes after cessation of stimulation.

of the respiratory movements caused by stimulation of the uncut vagus. If this were so, one would have expected a great diminution in the size of the left side of the thorax. This did not occur. So far as can be determined from a study of the film, a change in the capacity of the chest comparable to the change which took place in the bronchi did not occur. For this to have happened the chest must have had its diameter reduced to one-half; this would have reduced the capacity about four times. As it was, from the measurements made of the x-ray plate, the capacity could not have been reduced more than one-third. In this case, the trachea alone had its capacity reduced more than three times as the result of the change in size.

In the cat in figure 5 *A*, the cervical portion of the left uncut vago-sympathetic nerve was stimulated. *C* was taken during a stronger stimulus than that given while *B* was taken. It is to be noted that the thorax is longer and narrower in *C* than in *B*, but the trachea in *B* is nearly 1 mm. narrower than that in *C*. In each the bronchi have been extremely narrowed, out of proportion to the change in width of the chest when compared to *A*, which was taken after stimulation had ceased.

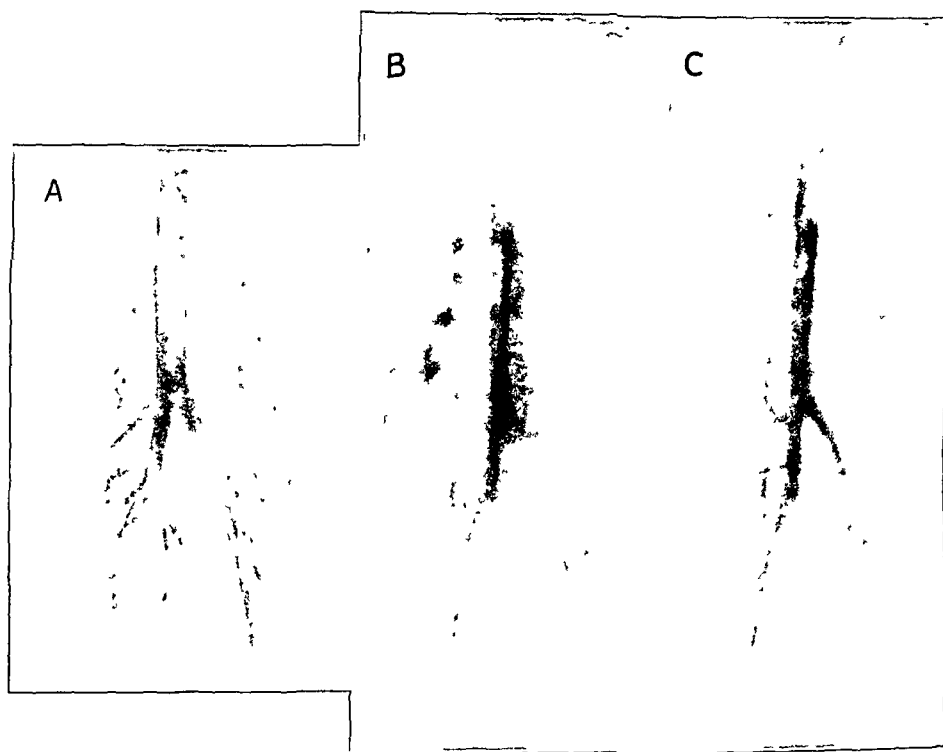


Fig. 5 (cat).—Anteroposterior position; *A* was taken at the end of a normal expiration, *C* during strong stimulation of the left uncut vagosympathetic nerve, and *B* during mild stimulation of the same nerve.

Cats lend themselves to this type of experimentation better than dogs, chiefly because the anteroposterior diameter of the chest of a cat is relatively short so that x-ray pictures may be taken with the animal lying on its back. Dogs, on the other hand, have a narrow chest but an anteroposterior diameter which is relatively great. Consequently it was usually necessary to take lateral plates.

Figure 6, taken of dog *J*, shows changes in the tracheobronchial tree. *A* was taken before stimulation. The right side of the chest was toward the plate; the trachea and right bronchus filled with bismuth subcarbonate are seen. *B* was taken five seconds after the beginning of stimulation of the right uncut vagosympathetic nerve. A marked general narrowing of the trachea and right bronchus is apparent. Both pictures were taken in expiration. By measurements of the two plates one cannot detect any difference in the size of the thorax.

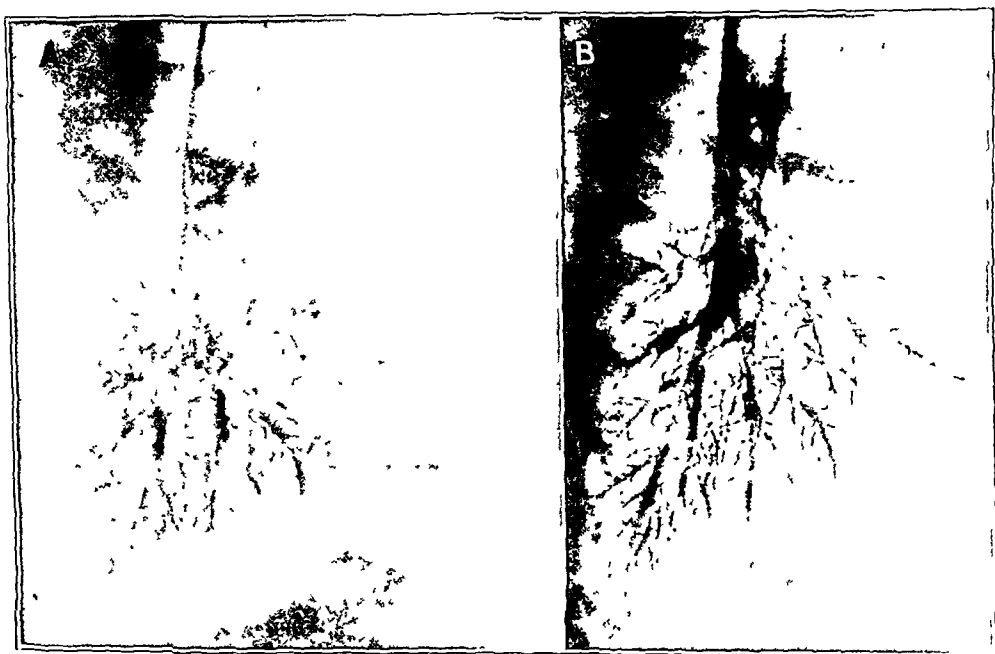


Fig 6 (dog).—Right side to the plate; *A* was taken before stimulation; *B*, five seconds after beginning of stimulation of the right uncut vagosympathetic nerve.

COMMENT

A roentgenologic demonstration is given of the changes in the size and shape of the tracheobronchial tree of cats and dogs which occur during inspiration and expiration. Also the changes which follow the stimulation of the cervical portion of the vagosympathetic nerve are demonstrated. The evidence here presented is not thought to be sufficient to make conclusions concerning the physiology of the tracheobronchial system. However, the method should lend itself well to further investigations of the bronchi of the intact animal.

3. EMPHYSEMA SIMULATING CARDIAC DECOMPENSATION *

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AND

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It has long been held that chronic emphysema sooner or later leads to cardiac failure. This statement appears in many modern textbooks of medicine. It is based largely on the presumption that as the lungs distend during the progression of emphysema, the pulmonary capillaries become stretched and narrowed. Consequently, the blood leaving the right ventricle meets peripheral obstruction, and added work is thrown on the right side of the heart which eventually hypertrophies, dilates and fails. This theory is founded on the clinical fact that patients with advanced emphysema usually have dyspnea on exertion, cyanosis and dependent edema, which are cardinal signs of cardiac decompensation.

In a previous study, fifty patients with long-standing bronchial asthma were examined. All of these had emphysema which, in some, was advanced. Particular attention was paid to the cardiovascular system, and little evidence of inherent cardiac damage was obtained. This led to the present study of the heart in chronic emphysema.

Sixty-six patients with emphysema were examined in detail. They were selected from moderately advanced to advanced cases. In almost all, the underlying etiology was some form of bronchial obstruction, such as asthma, chronic bronchitis or laryngeal compression. Again, particular attention was paid to the cardiovascular system. The only outstanding observations were a high peripheral venous pressure, and a lowered oxygen content of the arterial blood.

All these patients showed dyspnea on exertion and cyanosis. Dependent edema occurred in eighteen, and a history of this sign was obtained in fifteen others. These cases simulated cardiac decompensation. Nine patients with edema came to autopsy. In one there was hypertrophy of both the right and left ventricles. In eight no pathologic changes were found. In these, not only was there no right ventricular hypertrophy by measurement, but the normal ratio of right ventricular weight to left ventricular weight was maintained in each instance.

The finding of these normal hearts required an explanation of the signs of cardiac failure. Dyspnea and cyanosis may readily be attributed

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to the low vital capacity of the lungs and the impaired pulmonary ventilation that occur in emphysema. The edema is ascribed to the high peripheral venous pressure, and anoxemia, for the two factors most conducive to edema are increased capillary pressure and anoxemia, both of which occurred in these cases.

The reason for the high venous pressure was studied in dogs. A ball valve was fastened in the trachea and adjusted so that the amount of expiratory obstruction could be regulated. Within a short time, emphysema appeared; this was permitted to continue over a period of weeks. Intrathoracic and peripheral venous pressures were recorded periodically. Increased pressure in the thorax occurred early. As this advanced, the peripheral venous pressure rose proportionately. This is accounted for by the partial obstruction to the return of peripheral venous blood into the thorax, which results from increased intrathoracic pressure.

CONCLUSIONS

From this study, the following inferences are made:

1. Heart failure is not necessarily a consequence of emphysema.
2. In cases of marked emphysema, peripheral signs simulating cardiac failure are attributed to factors other than a damaged heart.
3. These factors are lowered vital capacity (dyspnea), deficient pulmonary ventilation (cyanosis) and an increased peripheral venous pressure associated with anoxemia (edema).
4. Heart failure and emphysema may coexist, as in senile arteriosclerosis. Here, emphysema is usually not advanced, and there is no evidence that it damages the heart.

4. EXPERIMENTAL ABSCESS OF THE LUNG FOLLOWING LIGATION OF THE PULMONARY ARTERY AND INCISION AND SUTURE OF THE PULMONARY PARENCHYMA *

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AND
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We hesitate to add further to the literature which concerns itself with the theory concerning the development of abscess of the lung. In attempting to attack this problem from various angles, many investigators have often disregarded striking clinical observations and facts; this is an endeavor to discover a method which when perfected would carry with it a guarantee of producing an abscess of the lung in practically every instance. By so doing they have endeavored to prove that certain postoperative complications, as for example, abscess of the lung, always result from a single mechanism. Others have gone further and have concluded that a given mechanism always operates and is common to other postoperative pulmonary sequelae. Such mechanically perfect experiments naturally add considerable weight to the explanation of how such conditions develop and point out how in many instances their occurrence may best be avoided. Such a simplification, although most desirable, is certainly not justifiable at the present time. We believe that abscess of the lung may develop in several ways. We wish to stand in the middle of the road.

The object of this paper is, therefore, not to introduce a new method, to formulate further burdensome theory or to draw any sweeping conclusions from the results which we have obtained. The purpose is rather to record observations as they occurred in the hope that our experiences may at some future time add to, or help to discard a link from, the chain of theory.

Our original studies were undertaken to observe the origin of the scar tissue in healing of the lung. They were stimulated more particularly in the light of the recent experiences of others who have questioned the previously accepted conception of the development and structure of the lung. We observed that simple incision and suture of the pulmonary parenchyma resulted in a scar which resembled a scar elsewhere on the body. Phrenicotomy performed on the corresponding side in no way affected the end result. These studies will be reported elsewhere.

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In the course of our investigations we found that ligation of the pulmonary artery and simple incision and suture of the pulmonary parenchyma were followed by the development of an abscess of the lung in the lobe so treated. We were frequently able to repeat this observation, as our recorded experiments will show. Explanation of much in this connection, nevertheless, still remains to be made. Among other things, our bacteriologic studies to date are as yet incomplete.

All experiments were performed on dogs under absolutely sterile conditions. The positive pressure apparatus of Erlanger-Gessel was employed.



Fig 1 (dog 117) —Abscess of the right lower lobe of the lung.

EXPERIMENTAL WORK

Dog 117 (2) —The pulmonary artery to the right lower lobe was ligated. A transverse incision, which included a large main bronchus, was made in the right lower lobe. The cut ends of the bronchus were allowed to retract and the lung was resutured. The dog was killed on the seventh day. An abscess of the right lower lobe of the lung was found (figs 1, 2 and 3).

Necropsy —The lung was quite firm. The suture line was intact. On cutting through the lobe on which operation had been performed, a definite abscess, 2 cm in diameter, was observed. Through this abscess ran the remains of a large bronchus which was plugged. The main bronchus just adjacent to the abscess was patent. The abscess, which was solitary, extended well out to the periphery of the lung. The pleura was free. No other abscess formation could be made out in any other part of the lung.

Microscopic Examination—The microscopic picture verified the gross observations. The lung tissue adjacent to the abscess is filled with a fluid exudate plus inflammatory cells and red blood cells. The wall of the abscess is made of fibrin, pus cells and cellular debris. All the parenchyma of the lung in this region is destroyed. The extent of the abscess corresponds more to the extent of the incision.

Comment—The extent of the lesion and the tremendous inflammatory reaction were strong points against a purely ischemic origin of the



Fig 2—Low power magnification. Photomicrograph of abscess noted in fig 1

lesion. All adjacent vessels contained blood. No large groups of bacteria could be discerned. The rest of the lung requires no description.

Dog B 16 (3)—The technic used was that of the foregoing experiment. For one week after the operation, this dog was quite ill. During this period it coughed, pus poured out of its nostrils, and it frequently sneezed. The condition was obviously not one of mere distemper, and the dog gradually improved. It was killed after one month. The wound was healed. Beneath it there was breaking down of tissue, that is, an abscess.

Microscopic Examination.—Sections taken from the right lower lobe revealed the following: The cells had lost their staining property. There remained only the ghost of alveoli, with solid masses of pus.

Dog A 1 (4).—The animal was killed on the seventh day. Abscess of the lung was found. There was a definite thickening of the remains of the alveolar wall about the abscess. Pieces of bronchus and lung tissue were removed at the time of operation and cultures were made from them. No growth was obtained. Pus obtained from the abscess yielded no organism.



Fig. 3.—High power magnification. Photomicrograph of abscess noted in figs 1 and 2.

Dog A 2 (5).—The animal was killed on the seventh day. Abscess of the lung was found. A culture of a portion of excised bronchus removed at operation showed no growth.

Dog B 25 (6).—The animal was killed on the twelfth day. Necropsy showed abscess of the lung (figs. 4 and 5). The right lung, which had been operated on, was riddled with abscesses. The wound was healed, but not as firmly as usual. The pleural cavity was free. The microscopic observations were those of typical abscess formation.

Dog B 17 (8).—The animal was killed on the fifth day. There was no evidence of abscess of the lung. The lung was grossly firm. The incision had healed.

There were no adhesions. There was considerable induration of the lung tissue distal to the incision. A large bronchus which had been intentionally cut across was plugged. There was a firm scar and no abscess.

Microscopic Examination.—There were exudate in the alveoli and blood in the region of the incision. There was not the actual connective tissue scar proliferation that was noted in the lungs in which the pulmonary artery was not ligated. The plugged bronchus contained cellular debris and pus cells.

Dogs 16 A (9) and B 3 (10).—Both dogs were killed seven days after the operation and both had an abscess in the lobe of the lung which had undergone operation.

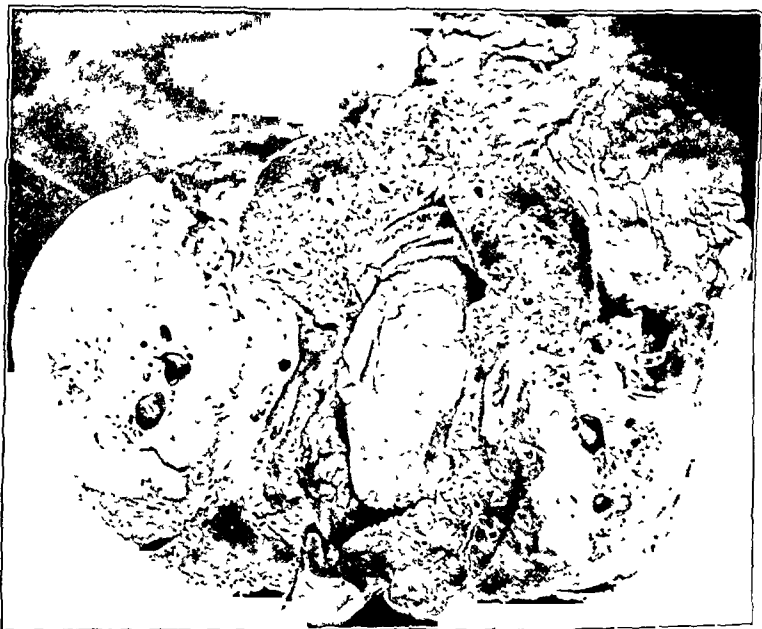


Fig. 4 (dog B 25).—Gross section of the right lower lobe cut in half, showing large abscess of the lung.

COMMENT

In a series of experiments in which ten dogs were employed, the pulmonary artery to the right lower lobe was ligated. The pulmonary parenchyma of the same lobe was incised for 3 inches (7.6 cm.). The incision included a large bronchus. An abscess of the lung (the right lower lobe) developed in eight of ten instances when the pulmonary artery was ligated and the pulmonary parenchyma incised and sutured. The scar healed in every instance. In no case did empyema develop. One dog showed the remains of an old abscess, another a lesion which was considered a healed abscess. Multiple abscesses in the lobe oper-

ated on were noted only once. The abscess was always found in the lobe which had been operated on, and never elsewhere. Its diameter in a few instances corresponded to the length of the scar, but the latter, as already noted, was free in every instance. It is to be noted that the bronchi which were cut across were allowed to retract. In three instances in which abscess of the lung developed, a portion of bronchus was excised at the time of operation and showed no growth. In two of these instances, culture of the abscess yielded only spore formers on one occasion. There was no growth.

Changes in the lung following ligation of the pulmonary artery have been described by Schlaepfer and others. He noted fibrosis of the lung following ligation of the pulmonary artery, especially when this proce-



Fig. 5 (dog B 25).—Photomicrograph of high power magnification of abscess noted in fig. 4.

dure was combined with phrenicotomy and with partial occlusion of the pulmonary veins. Schlaepfer observed that after ligation of the pulmonary artery a stasis takes place on the alveolar side of the pulmonary veins with a resultant exudation of serum, erythrocytes and leukocytes into the alveoli and interstitial tissue. At the beginning there is also an increased flow of lymph.

William Snow Miller long ago demonstrated the fact that the bronchial blood vessels are directly connected with the pulmonary vein. That fine, barely demonstrable, yet adequate, anastomoses may take place between arteries and veins was shown by Hayer.

Virchow's investigations on hemorrhagic infarcts of the lung led him to conclude that the interruption of a branch of the pulmonary

artery in no way influenced the nutrition of the pulmonary parenchyma. The bronchial arteries apparently give off important nutrient branches. This view is not in accord with that of Cohnheim and Litten, who did not feel that the bronchial arteries were absolutely adequate in this respect.

Chjrzontschewsky experimentally injected a dye into the circulation after having ligated the main branch of the left pulmonary artery. He found the substance not only in the bronchial arteries, but also in the branches of the artery which had been tied off and also in the veins. He therefore concluded that this demonstrated the presence of a capillary network. Küttner's observations in this respect were similar.

Konaschko was able to prove rather conclusively that adequate communications exist between the pulmonary artery and the bronchial arteries. He was able to fill the mediastinal pleural branches of the bronchial artery by injecting the pulmonary artery. He also observed that similar fine communications existed in the walls of the bronchi. His observations in general substantiate many of those previously made by Zuckerkandl.

It would therefore seem rather certain that adequate nutrition of the pulmonary parenchyma exists following ligation of the pulmonary artery, at any rate sufficiently adequate nutrition, under previously normal conditions, to prevent the occurrence of a hemorrhagic infarct. It is interesting in this connection to consider the work of Rose, who considered the lung as essentially a vascular organ.

We observed no appreciable increase in fibrous connective tissue in the lung over periods up to four weeks following ligation of the pulmonary artery. No abscess formation followed this procedure.

The corresponding lobe did not decrease in size, nor did the alveoli appear to be smaller. Other changes observed corresponded to those already described by Schlaepfer.

Hasslinger and Sternberg studied the flora of the tracheobronchial tree in the living person. These investigators also studied the flora of the tracheobronchial tract of the dog. They were able to show that use of cocaine or of cocaine and epinephrine somewhat retards the growth of bacteria from twenty-four to twenty-eight hours but does not kill them. They observed their cultures for eight days. Their technique was extremely careful and was carried out through a bronchoscope. They recovered streptococci, staphylococci, rods and various saprophytes from the subglottic space of seven dogs. The secretions from the trachea beyond the bifurcation and from the main bronchi were in every instance sterile, both in patients and in the dogs.

In our experiments, six dogs were killed on the seventh day. All these dogs had developed an abscess of the lung, one of which was

healed. Two dogs were killed after one month. One of the dog's lungs in this group showed a healed abscess, the lungs of the remaining dogs, no abscess. One dog was killed on the fifth day and showed no evidence of abscess of the lung. The tenth dog was killed on the twelfth day and showed multiple abscesses of the lung. We injected known organisms into a bronchus and then ligated the pulmonary artery in one instance. We were able to recover the same organism from the pneumonic areas which resulted. As to the *raison d'être*, we can at the present time only theorize. Simple incision and suture of pulmonary parenchyma is not followed by the development of an abscess of the lung. Similarly, simple ligation of the pulmonary artery shows no such change. The combination of both procedures, in our experience, frequently results in the development of an abscess of the lung. From the experience of Haslinger and Sternberg and from our own in three instances, we know that the bronchi are apparently normally sterile. It is possible, however, that the trauma to the lung puts it somewhat at rest, and therefore it may not be unlikely that organisms may reach the lung, either from the mouth or through the circulation. Be this as it may, the contents of the cut bronchus can pour into the parenchyma. Such bronchi have been observed to be plugged with pus. The presence of blood from the original operation must also be considered as a possible factor. The abscess formation could not be attributed to faulty technic or to a foreign body, such as silk, which was the suture material used. The ligation of the pulmonary artery may slow the circulation somewhat. Our bacteriologic studies are as yet incomplete. No virulent organisms have been recovered, however, from the abscesses which resulted. The lobes operated on as described functioned perfectly. We thus have a combination of circulatory and "aspiratory" factors, and, as has been suggested by others who have worked with noninfected bland emboli, it would perhaps seem that abscess of the lung, like so many other lesions, may not only result from several mechanisms, but that its formation requires a combination of factors.

SUMMARY

1. In ten dogs, ligation of the pulmonary artery to the right lower lobe and simple incision and suture of the pulmonary parenchyma of the corresponding lobe was followed by the formation of an abscess of the lung in eight instances.
2. No appreciable increase in fibrous connective tissue was observed in the lung over periods up to four weeks following ligation of the pulmonary artery.
3. The corresponding lobe did not decrease in size, nor did the alveoli appear to be smaller.

4. Simple incision and suture of the pulmonary parenchyma resulted in a scar which resembled a scar elsewhere in the body and was not followed by the development of an abscess of the lung. It is to be noted in this connection that phrenicotomy performed on the corresponding side apparently in no way influenced the end result.

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5. THE ORIGIN OF SCAR TISSUE IN HEALING OF THE LUNG*

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AND

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These studies are concerned with the origin of scar tissue in healing of the lung. They were undertaken chiefly because of the recent experiences of others who questioned the previous conception of the development and structure of the lung. All experiments were performed on dogs under sterile conditions. The positive pressure apparatus of Erlanger-Gessel was employed. The first group of experiments illustrate the effect of simple incision and suture of pulmonary parenchyma.

SIMPLE INCISION AND SUTURE OF PULMONARY PARENCHYMA

Dog 138.—A single incision, 2 inches (5.0 cm.) long, which ran at right angles to the axis of the main bronchus was made in the right lower lobe of a dog's lung on Dec. 31, 1928. This incision included several blood vessels and bronchi. The animal showed no discomfort and was killed on the tenth day, by means of an overdose of ether. The chest cavity was reopened under positive pressure. The incised lobe was previously observed to function perfectly. There were no adhesions; the suture line had healed perfectly.

Microscopic Examination.—Microscopically, the lung was normal throughout in every respect. There were no abnormal cells and no exudate. The scar resembled a normal scar which might be found on any other part of the body. The pulmonary parenchyma distal and proximal to the scar looked alike. There was only slight local compression of alveoli, which could be attributed to the contraction of the scar.

Dog 139.—Another dog operated on as described was killed on the fifteenth day. A few fine adhesions could be noted, but only where the lung had been handled by gauze, which was away from the incision. The incision was smooth. The entire lung contained air. There were no evidences of mediastinal or subcutaneous emphysema.

Microscopic Examination.—Smaller bronchi were observed to have been cut across and were somewhat collapsed. There was slight pulmonary emphysema about the scar, but this was in all probability due to the fact that the lung had after removal immediately been fixed by injecting a diluted solution of formaldehyde into the bronchial tree. There was active proliferation about the scar. The origin of the scar tissue could not be definitely determined.

Another dog operated on in a similar manner developed an empyema and died on the fourth day. The line of incision had not broken down. No bronchial fistulas could be demonstrated. A fistula may, however, have been coated over by exudate. The right lung showed evidences of pneumonia. There was no abscess formation in the lung.

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The fourth dog in this series of experiments was killed on the fifth day. The observations were essentially those noted in the first two experiments.

The suture line was in a moderately advanced stage of healing. A slight extravasation of blood into the wound could be noted. Some small bronchi which had been previously cut across were caught in the scar and were partially collapsed. All adjacent blood vessels were dilated and filled with blood.

Comment.—A scar in the lung, the result of a simple incision and suture of pulmonary parenchyma, resembles a scar elsewhere on the

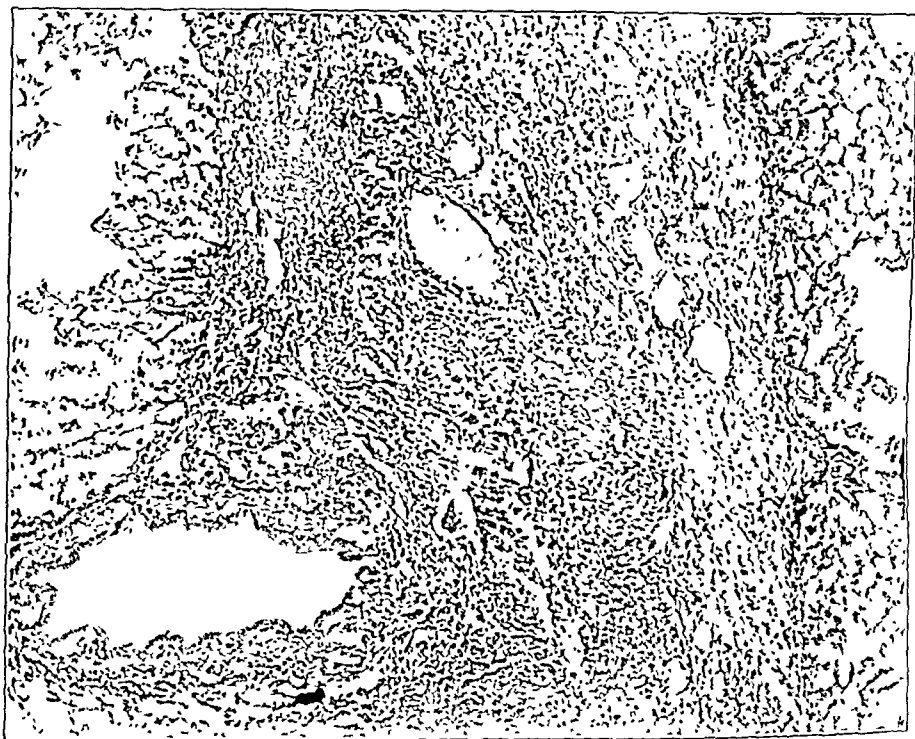


Fig. 1 (dog 138).—Photomicrograph showing a ten day old scar in lung. This scar followed a simple incision and suture of the pulmonary parenchyma. It is made up of connective tissue and shows moderate round cell infiltration. Normal air-containing alveoli are seen on either side of the scar. An adjacent bronchus is unaffected.

body. Except for the presence of adjacent collapsed alveoli, which are alveoli caught in the contracting and retracting scar, no differences on ordinary histologic examination can be noted. The usual methods of examination do not permit one to ascertain the origin and source of the scar tissue. Simple incision and suture of normal lung tissue under sterile conditions is not followed by abscess formation.

SIMPLE INCISION AND SUTURE OF PULMONARY PARENCHYMA
FOLLOWED BY INTRATRACHEAL INJECTION OF
TRYPAN BLUE

The following experiments differ from those already recorded only in that on the first, second, third, fourth and fifth postoperative days the dogs experimented on received an intratracheal injection of 5 cc. of a 1 per cent solution of trypan blue. This first dog was killed on the tenth day. This was exactly three days after the last injection of trypan blue.

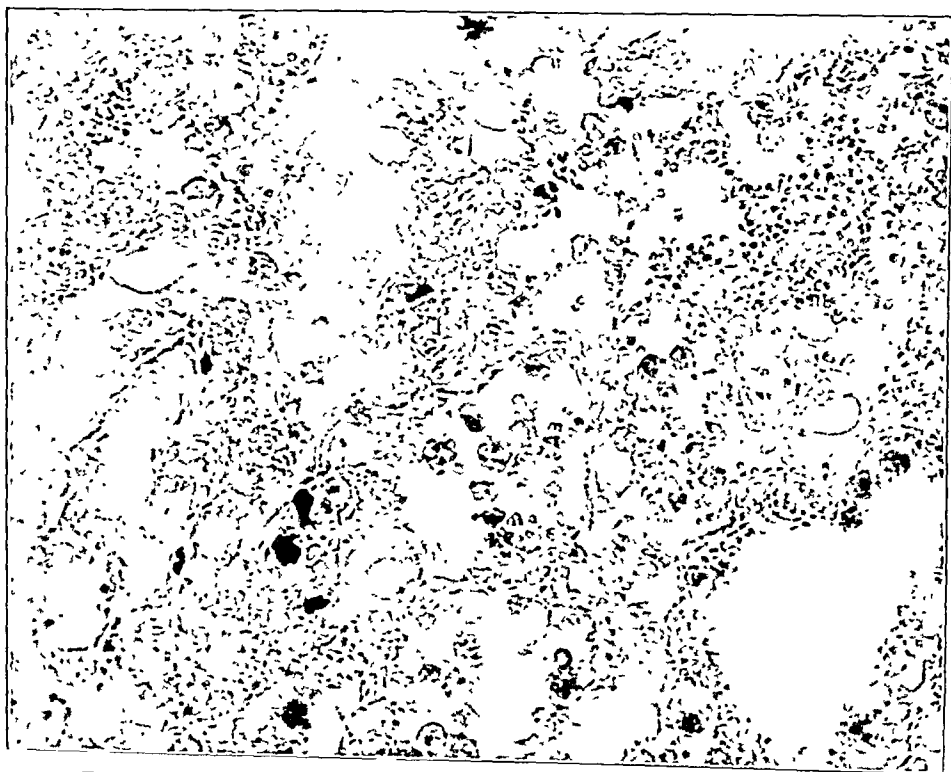


Fig. 2.—Note macrophages containing trypan blue. The smaller cells seen in the right upper quadrant are erythrocytes. Low magnification.

Grossly, such a lung was nonadherent. The suture line was clean and healed. Most of the trypan blue was in the right lower lobe; but relatively little was in the region operated on, namely, the right middle lobe. The lung felt firmer and more solid than normal.

Microscopic Examination.—The incision in the lung showed all the signs of active healing. Considerable patchy cellular exudate (red blood cells and mononuclear cells) could be observed throughout the whole right lung; this was most marked in the "incised" lung, particularly in the areas which contained trypan blue.

Dog 340.—The right lower lobe was incised and sutured. The subsequent technic was as already noted.

On March 11, this dog was given 20 cc. of trypan blue intratracheally.

On March 12, the left side of the chest was opened and the left lower lobe was operated on in a similar manner. A wedge of lung tissue was excised from this lobe. On March 13, 14 and 15, the animal was given doses of 10 cc. of trypan blue intratracheally in an attempt to demonstrate the histiocyte reaction following the injection of this dye.

The dog was killed on March 16, that is, five weeks after the first operation and four days after the second operation. Both lungs were blue and fairly firm. A hematoma could be seen in the left lower lobe. There was no inflammatory reaction about the hematoma, which lay distal to the scar which was four days old.

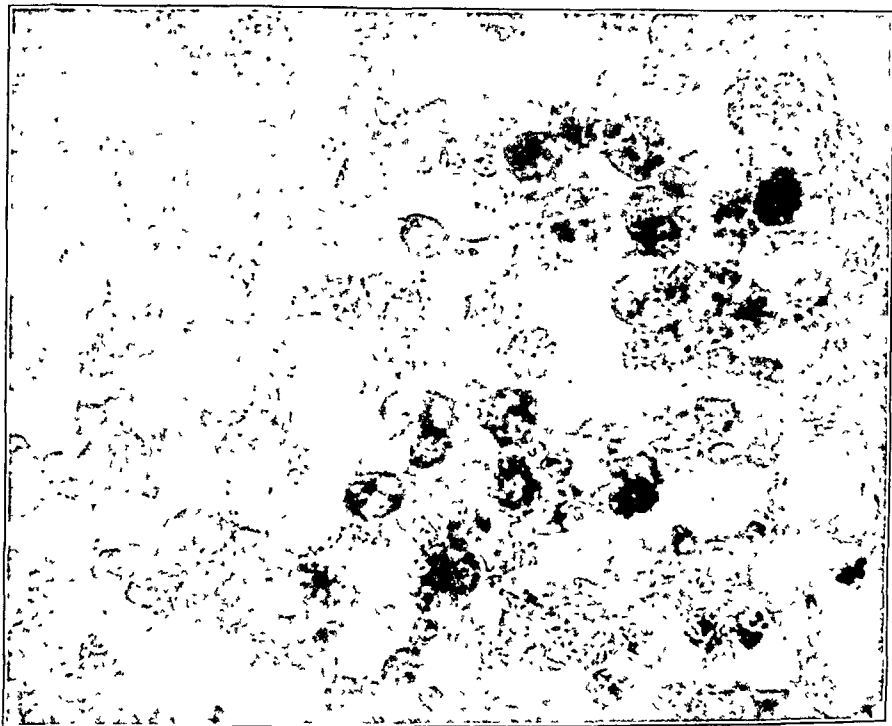


Fig. 3.—Photomicrograph of same field as that in figure 2. High magnification.

The question might be raised as to whether additional factors, such as slowing of the circulation, might not under favorable circumstances render such a hematoma susceptible to secondary infection.

The scars in both lungs were healed. No abscesses could be noted.

Microscopic Examination.—Section A, taken from the left lower lobe at the time of the second operation, which was performed twenty-four hours after the injection of trypan blue, showed considerable exudation of cells of all kinds.

Sections from the left lower lobe, taken four days later, showed that the exudate was more extensive than that noted in section A. It is to be appreciated, however, that the dog in the meantime received additional injections of trypan blue. More pigment was therefore to be observed in the cells, many of which seemed to plug the alveoli.

Sections taken from the right lung at necropsy showed a healed scar. There were still evidences of the exudation of cells, engorgement of interalveolar capillaries with blood, and areas in which the general arrangement of inflammatory cells resembled pneumonia. A microscopic section from the right upper lobe gave the same picture of a "patchy pneumonia."

No pigment cells were observed in the scar.

Dog 300.—On Feb. 22, 1929, a simple incision and suture of the pulmonary parenchyma and intrathoracic phrenicotomy on the right side were done. On March 11, 20 cc. of a 1 per cent solution of trypan blue was injected intratracheally. On March 12, a wedge was cut out of the left lung. On this occasion the lungs were quite blue and felt irregularly firm, much more so than a normal lung. From March 12 to 15, 10 cc. of trypan blue was given intratracheally. The animal was killed on March 16, which was twenty-two days after the first operation and four days after the second operation, which was on the left side.

The right side of the diaphragm showed the effects of the phrenicectomy. It was thin and atrophic.

There was a perfect scar in the right lung. There was some hemorrhagic discoloration about the scar in the left lung.

No abscess formation or pneumonic process could be noted in either lung.

Microscopic Examination.—A specimen taken at second operation showed what would be expected twenty-four hours after the injection of trypan blue. There was a patchy pneumonic-like process. The blood vessels were engorged. Patchy exudation was most marked about the bronchi, which also contained inflammatory cells.

The injection of trypan blue into the lung produces patchy pneumonic-like areas. In these areas only little trypan blue can, however, be observed. Only an occasional phagocyte which had ingested trypan blue was observed in the areas from which sections were taken. Yet such an area of the lung is quite blue, firm and, as already mentioned, shows microscopically only a little trypan blue.

A section taken from the left lung (the same site as that of the aforementioned section) four days after the second operation showed active fibrous reaction. There was considerable leakage of blood into the wound, around which fibrous tissue reaction attempting to wall it off could be noted. There were also many inflammatory cells here. The lung tissue about the scar contained air. There was a large number of scattered cells in the alveoli and mononuclear cells which appeared to come from the alveolar wall. There were practically no pigment cells in the scar tissue.

Sections from the right lung, which was operated on five weeks previously, showed complete healing of the scar. Many cells loaded with pigment were to be seen in the alveoli, also a few in the scar.

Section 300 E was taken from the right upper lobe, which was normal except that it had received injections of trypan blue. This lung showed the "pneumonic-like" processes alluded to, and many "dust cells" which contained blue pigment.

COMMENT

In the earlier experiences with vital staining in the study of the reticulo-endothelial system of the body, it was noted that the lungs remained singularly free from pigment-laden macrophages or showed just a few such cells after the intravenous or intraperitoneal injection of various dyes. Certainly such lungs showed proportionately much less

pigment than was found in other organs of the body, notably the liver. The few pigment cells found in the lung were grouped about the larger blood vessels. From these observations it was concluded that the macrophages did not originate in the lungs, and that these organs could not be classed as a part of, or considered to contribute to, the reticulo-endothelial system. Because the pigment cells seen in the lung were about the blood vessels, it was thought that they arose from the capillary endothelium.

Fried¹ more recently reconsidered the macrophage reaction in the lungs by injecting vital dye and oil intratracheally. He found that there is abundant proliferation into the alveoli of mononuclear cells laden with pigment after the injection. He showed that they came from the cells lining the alveoli. They corresponded morphologically and physiologically to the macrophages of the reticulo-endothelial system. He thus concluded that the lung has an active defense mechanism concerned with the proliferation of these cells, and that the alveoli are not lined with epithelium but with cells having the properties of macrophages. The latter, then, do not come from the capillary endothelium but from the alveoli. The reasons why this reaction is not seen after intravenous or intraperitoneal injections of vital dye are: (1) The dye is diluted; (2) the Kupffer cells of the liver pick it up and so prevent its entering the lung, and (3) a large part of the dye is excreted in the feces, urine and bile. Other observations on the lungs so treated were: thickening of the alveolar walls; the filling up of alveoli with these cells, and their coalescence to form patches resembling those seen in bronchopneumonia.

In trying to determine the origin of the cells forming the scar in the parenchyma of the lung, we wondered as to the rôle played by the cells that line the alveoli and proliferate abundantly. The thought occurred that they contribute to the formation of the scar. Dogs therefore received intratracheal and intravenous injections of 10 cc. of a 1 per cent solution of trypan blue. The injection was given slowly. The animals were held in the upright position while the dye was given, and for ten minutes afterward. On the following day, the chest was opened under ether anesthesia administered by means of the positive pressure apparatus. The lungs were found to be somewhat firmer than usual and to be stained in varying intensity in irregular patches. The incision into the parenchyma was always made in the right lower lobe as described. A wedge of lung tissue was cut out from the edge of the incision for microscopic study at the time of operation. The wounds in the parenchyma and chest were then sutured. The chest was closed in layers. As all incisions in the larger muscles were made in the direc-

1. Fried, B. M : The Defensive and Metabolic Apparatus of the Lungs: The Lungs and the Macrophage System, *Arch. Path.* 6:1008 (Dec.) 1928.

tion of their fibers, which were then retracted, a good closure was insured. On the first, second and third postoperative days, these dogs each received 10 cc. of the 1 per cent trypan blue solution intratracheally. They were killed on the fifth or seventh day after operation. Just before death the lungs were functioning, and no adhesions were seen at the suture line. The lungs were firmer than normal and stained irregularly with the blue dye. On section, no abscesses were found, and the pinkish-white scar could easily be made out.

The microscopic observations in these lungs coincided with those described by Fried:² areas of proliferation of alveolar lining cells, the presence of pigment in these cells, thickening of the alveoli and coalescence of areas of proliferation into pneumonia-like patches. The striking observation, as far as we are concerned, was the absence of macrophages, at least of pigment-containing cells, even in the early scars.

According to Fried's observations, we should have found large numbers of these phagocytic cells among the devitalized cells and the blood pigment found in the edges of the incision into the parenchyma of the lung. A few such cells were seen near the scar but not in it. Evidently such phagocytic cells do not wander far from the alveoli in which they arise, or else the stimulus of simply incising the lung is not sufficient to attract them to the scar. We believe that the scar which develops following a simple incision into the lung is formed from the fixed tissue cells arising from the supporting framework of the lung, and that the cells lining the alveoli do not contribute to this scar. The function of the macrophages in this connection seems to be rather more one of defense against organisms or particulate matter introduced directly into the alveoli.

SUMMARY

Some observations have been made concerning the origin of the scar tissue in healing of the lung. A scar in the lung, the result of a simple incision and suture of pulmonary parenchyma, resembles a scar elsewhere in the body. The injection of trypan blue into the lung produces patchy, pneumonic-like areas. Practically no pigment cells are to be found in the scar, even early in the process. It would seem that the scar arises from the fixed tissue cells of the supporting framework of the lung, and that the function of the macrophages is rather one of defense against organisms or particulate matter which are introduced into the alveoli.

2. Fried, B. M.: The Origin of Histiocytes (Macrophages) in the Lungs, *Arch. Path.* 3:751 (May) 1927.

6. THE BACTERIAL FLORA OF TREATED AND UNTREATED ABSCESSES OF THE LUNG *

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In the majority of cases of chronic abscesses of the lung reported in the literature, the bacteriologic study has been limited to the preparation and examination of stained smears for the presence primarily of fusiform bacilli and spirochetes, the diagnosis being made on the satisfactory demonstration of these organisms in conjunction with the clinical observations. Chief clinical interest in the so-called "etiology" of this condition has been in whether it results primarily from the aspiration of infected material from the mouth and nasal passages or from the introduction of infected emboli into the blood stream. In contradistinction to the study of the predisposing factors, complete bacteriologic studies of the bacterial flora in these cases have been surprisingly few in number. In pathologic conditions such as abscesses of the lung, it is extremely difficult to select any one organism or even a number of organisms as the etiologic factors. It is of importance, however, to study the bacteriologic flora of such abscesses, as through this study one may possibly determine the source of infection and be enabled to guard against the initial infection.

In many of the bacteriologic studies made, little information has been obtained because of the failure of investigators to include in their technical methods anaerobic as well as aerobic methods of study. In the last few years increasing emphasis has been directed toward the rôle of anaerobes in the production of abscesses of the lung, this evidence all pointing toward the importance of a proper study of the anaerobic as well as of the aerobic flora of material from these lesions. The bacterial flora of abscesses of the lung can be determined only by an increasing number of careful studies of infected material, in which the importance of anaerobic as well as aerobic flora is taken into consideration. The data on which the present report is based were secured from the study of a large series of cases of abscesses of the lung in Barnes Hospital, twenty-seven of which were selected as meeting what were believed to be the primary requirements for an accurate study of the bacterial flora of this condition; namely, freedom of the material studied from external contamination, and an immediate plating of the material following its withdrawal from the body.

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The material from these patients was secured and prepared for study in the following ways: (1) At Operation: In these cases, the pus was aspirated under aseptic precautions the moment the pus cavity was opened, immediately placed in a sterile tube kept at 37 C., and without further delay taken to the laboratory for examination. Material from several of these patients was also introduced into the lungs of dogs in an effort to produce abscesses of the lung by experimental methods.¹ Pus secured in this manner was not treated in any way other than to wash thoroughly, in several changes of warm sterile saline solution, any granules which might be found, in order to remove liquid pus which might adhere. Both the granules and the liquid portions of the pus were then separately plated on blood agar, and immediately incubated at 37 C., under both aerobic and anaerobic conditions. Plates were incubated under anaerobic conditions in the phosphorus anaerobic jar previously described by me.² Smears of both granules, if present, and the liquid pus were prepared and examined after staining by Gram's method, with gentian violet, and by the method of Fontana.

(2) By Postural Drainage: Following a cleaning of the mouth with a suitable wash, the patient was inclined with the head lower than the feet, so that the abscess pus drained freely from the mouth. The first portions were discarded and the material to be studied was collected in a sterile container, transferred immediately to the laboratory and treated as described.

(3) By Coughing While in a Reclining Position: The mouth was washed as before; the patient was turned on his side and was instructed to cough. By this method, certain samples of pus were found to be grossly contaminated with saliva and sputum from the upper respiratory passages, often sufficient in amount to cause it to separate into three layers as is often described in the literature. Such material is almost worthless for examination. In some cases, therefore, repeated samples were secured before a satisfactory one was obtained. If the material appeared to be largely saliva, it was discarded and another sample was secured. Only when a very small amount of saliva was present in the pus was the sample deemed representative enough to be used in this study. On arrival at the laboratory, the sample was placed in thin layers in a petri dish, the pus being separated from any saliva present, and thoroughly washed in repeated changes of sterile saline solution. The granules were picked out by means of a needle and treated similarly, following which the usual smears and cultures were made.

1. Allen, Duff S.: Etiology of Abscess of the Lung, *Arch. Surg.* **16**:179 (Jan.) 1928.

2. Varney, Philip L.: A Simple Method for Cultivating Anaerobes by Means of Phosphorus, *J. Lab. & Clin. Med.* **11**:1183, 1926.

(4) By Swabbing, Following Operation: This method was used when it was found desirable to check the progress of the disease following operation, and when none of the methods previously described could be utilized because of their danger. A sterile, tightly rolled cotton swab was introduced deep into the wound; the patient was told to exhale, and the pus which was forced out was collected on the swab. The amount of material secured in this manner was often very small, and a decided change in the bacterial flora could often be demonstrated.

McNeill³ and others have reported the rapid disappearance of spirochetes from saliva and pus secured from abscesses of the lung when the material is allowed to stand for a few minutes or hours in an open container. In the early stages of this work, therefore, before this phenomenon could be investigated, the first procedure on securing the sample was to prepare smears of it, in the belief that otherwise no spirochetes might be found. Early results seemed to substantiate the observations of these investigators; like them, I could find no spirochetes in the sputum after it had stood for a short interval following its withdrawal from the body. This fact necessitated, therefore, the rapid preparation of smears before cultures were made. In a later study relative to the disappearance of spirochetes from the pus, it was found that they could usually be demonstrated, if present in more than minute numbers in the original material, for as long as forty-eight hours after their withdrawal from the body, and that by preparing smears several hours after the withdrawal of the pus one could demonstrate them in their original concentration, providing that the proper material was chosen for examination. Most samples of unaltered pus from abscesses of the lung are rather tenacious or sticky, and any suspended matter will remain evenly distributed throughout. The spirochetes in the samples of pus studied in this series of cases were found almost exclusively in small, minute granules, which were soft to hard, cheesy or calcareous, white to dark brown masses composed of bacteria and which varied in size from a fraction of a millimeter to several millimeters in diameter. These granules are almost invariably present in chronic or far advanced cases of abscesses of the lung and bronchiectasis. They usually have a foul, intense odor, reminiscent of that produced by *Bacillus melanogenicum*, one of the organisms to be described. When examined under the microscope these masses are often found to consist of enormous numbers of spirochetes, which in wet preparations are actively motile, mixed with streptococci and varying numbers of gram-negative and gram-positive cocci of several species. Due to the semiliquid state of the material surrounding them, these granules usually remain evenly

3. McNeill, Clyde: Pulmonary Infection with the Spirochaetae and Fusiform Bacilli of Vincent, Bull. Johns Hopkins Hosp. 35:368, 1924.

suspended for a short period of time following the withdrawal of the pus, and are readily withdrawn by the inoculating loop when the material is smeared out, so that if any granules are present spirochetes will usually be found. After standing for a short period of time, however, the pus becomes quite liquid, owing to the action of its proteolytic enzymes, and as a consequence the granules settle out, carrying the spirochetes with them. It is therefore of the greatest importance to examine the pus for the presence of these granules, for it is here and usually only here that the spirochetes may be found. If they are apparently discovered in the liquid portions of the pus, it will usually be found that one has accidentally picked up a small granule and smeared it out together with the liquid portions of the pus. Knowing the location of the spirochetes, and that they can still be found many hours after the withdrawal of the pus, it is of advantage first to plate out the material as rapidly as possible, thus giving no chance for a change in the bacterial flora, and subsequently to prepare the smears immediately after the plating. In this work, the material was first thoroughly washed; then the granules and liquid portions were plated separately on special blood agar, consisting of 1 per cent proteose peptone, 0.5 per cent sodium chloride, 0.3 per cent beef extract and 1.7 per cent dried agar-agar adjusted to p_{H} 7.4. In each of the cases in this series, the material was plated within fifteen minutes after its withdrawal from the body, and most of the platings were completed in from five to ten minutes; thus there was little chance for any change in the bacterial flora, through either the multiplication or the death of any of the micro-organisms present. It was found by cultural tests that the fusiform bacilli and spirochetes often remained alive for as long as twenty-four hours after the collection of the samples; hence it is safe to assume that the brief exposure of the samples to air had little deleterious effect on the anaerobic flora.

The pus or granules were streaked out on plates by means of a special machine streaking,⁴ as it had been found almost impossible to get representative results on repeated culture when hand streaking methods were employed. When streaked by the aid of the machine, the tenacious, tough material could be distributed evenly, owing to the greater pressure of the contaminated inoculating spatula which could safely be applied against the agar as compared with the pressure possible with hand streaking; this method thoroughly liberated the imprisoned bacteria and gave rise to an evenness and degree of distribution not possible to obtain by hand methods. Many of the bacteria repeatedly found in large numbers following machine streaking could scarcely be found

4. Varney, Philip L.: A New Spiral Streak Plate Method of Isolating Bacteria by Means of an Inoculating Machine, *J. Infect. Dis.* **41**:190, 1927.

following hand streaking methods. This was especially true in the study of the granular masses, for these must be subjected to a severe grinding action before they become sufficiently broken up to form well isolated colonies. Owing to this lesser grinding action, hand streaking methods gave entirely different and much less consistent results than those produced by machine streaking, and fusiform bacilli were often not found on plates streaked from material that was positive by microscopic tests.

Aerobic plates were examined in twenty-four hours and their bacterial population recorded, following which they were reincubated twenty-four hours longer and reexamined to see if any further changes had resulted. Changes seldom occur after forty-eight hours, however, even though the plates are incubated for as long as one week, and all the essential data can be secured within this period of time. The anaerobic plates incubated in the phosphorus anaerobic jar were first examined after forty-eight hours, as the colonies of fusiform bacilli, streptococci and pneumococci, if present, are most characteristic at this time. They were reexamined after a period of incubation of from one to two weeks for the final record as to the presence of *B. melaninogenicum* and any spirochetes which might have grown, or of any other slowly growing organism.

In this work, an attempt was made to study as closely as possible the aerobic and anaerobic bacterial flora present in the pus from chronic abscesses of the lung, especially in regard to the presence of *Bacillus fusiformis*, spirochetes, streptococci and *B. melaninogenicum*. While the first three organisms are familiar to all, the latter organism is comparatively unknown; hence a brief description of it may be of interest.

BACILLUS MELANINOGENICUM

Oliver and Wherry⁵ were the first investigators to study and name this organism. They noticed in cultures from the human body a minute, strictly anaerobic, nonmotile, polymorphic gram-negative rod measuring 0.8 by 1 to 3 microns, which, when grown under anaerobic conditions on mediums containing hemoglobin, produced after rather an extended period of incubation intensely black colonies which rapidly removed the last vestiges of hemoglobin from the plate, leaving it entirely colorless, similar to a plain agar plate. Because of the nature of the pigment, which they believed to be melanin, they named the organism *B. melaninogenicum*. Burdon,⁶ who has worked extensively with the organism in this laboratory, found it difficult by plate methods of isolation and

5. Oliver, W. W., and Wherry, W. B.: Notes on Some Bacterial Parasites of the Human Mucous Membranes, *J. Infect. Dis.* **28**:341, 1921.

6. Burdon, Kenneth L.: Bacterium *Melaninogenicum* from Normal and Pathologic Tissues, *J. Infect. Dis.* **42**:161, 1928.

study to isolate the organism in pure culture, as it grows in symbiosis with other organisms to a remarkable extent. He found the growth of strictly pure cultures to be slow, and that when so growing, the hemoglobin substrate was destroyed only to a slight extent. A small amount of contamination, however, far too little and in too intimate a mixture to be detected by a casual bacteriologic examination, would markedly stimulate the rate of growth of the organism, as well as enable it to hemolyze blood and destroy all color in blood agar plates within a short time.

Burdon secured rapid growth in mixed cultures; the development of the organism was indicated by the formation of a dark brown or black colony containing large amounts of an amorphous, extracellular, melanin-like pigment. In most cases the first trace of melanin was apparent after five or six days in primary cultures, although if the organisms were numerous the pigment might show up as early as the second day (forty hours) or, if the organisms were few, as late as the sixteenth day. The pigmented colonies of the organism grew in, on, over the top and around the colonies of other bacteria, which reached their maximum development long before the colonies of *B. melaninogenicum*.

Burdon found the organisms rather widely distributed about the body, and found them also in certain lesions of the lower animals, such as dogs and guinea-pigs. He found a close correlation between the number of colonies of *B. melaninogenicum* growing in the culture and the cleanliness of the organ from which the culture was made. The organism was present in all mouths; while present in only small numbers in normal mouths, so that a long and careful search was required to find it, it was exceedingly numerous in septic conditions such as pyorrhea alveolaris, in which it could be and was used as an index of the severity of the lesions.

The organisms were frequently found about the genitalia of both male and female patients, the relative number present being directly proportional to the lack of cleanliness of the parts or to the severity of the lesions, if any were present. In patients from the ward or the clinic, the organisms were abundant, but in private patients, who were obviously much cleaner as determined by inspection, few organisms were found. Schwarz and Dieckmann⁷ obtained *B. melaninogenicum* from nine blood cultures of patients suffering with puerperal fever, the organisms being identified by Burdon, and found the organism in 90 per cent of their routine uterine cultures.

In a study that I made, in 1926, of sixteen excised tonsils, reported by Burdon,⁶ *B. melaninogenicum* was found in every case, the plates

7. Schwarz, O. H., and Dieckmann, W. J.: Puerperal Infection Due to Anaerobic Streptococci, Am. J. Obst. & Gynec. 13:467, 1927.

made from the infected tissues showing from only a few to a great majority of colonies of the organism. Here again the numbers were proportional to the severity of infection, as determined by a study of the gross lesions of the excised tissues. Badly infected tonsils, especially those also containing large tonsillar granules within their crypts, showed large numbers of the organisms, whereas only a few black organisms were found in the apparently normal tonsils. Tonsillar granules were frequently found in the severely infected tonsils, and it was in these granules that *B. melaninogenicum* was most abundant. Some of these granules were so large that, unless preventive measures had been used, they might readily have been aspirated during operation, thus possibly giving rise to infections of the lungs. I found the flora of these granules to be almost exactly the same as that present in granular material in pus from abscesses of the lung, and it is my belief that abscesses of the lung following tonsillectomies may very likely result from the aspiration of such material.

No black organisms were found in cultures from the hands or fingernails of five persons examined, or from the axillae of five persons examined.

Fecal material from four infants less than 14 days old contained considerable numbers of *B. melaninogenicum*, but specimens from four other infants were negative. Cultures were taken from the feces of fifteen adults; ten cultures were positive, and all showed a fairly large number of the organisms, indicating that once they pass into the alimentary canal, they may persist throughout the entire tract.

Both aerobic and anaerobic cultures were made in a small series of cases of cervical abscesses studied at Barnes Hospital. *B. melaninogenicum* was found in every case in rather large numbers, in some cases constituting a majority of the organisms found. The pus was a deep chocolate-brown, with an odor similar to that produced by mixed cultures of *B. melaninogenicum*. In addition to this organism, fusiform bacilli, spirochetes and streptococci were also encountered in these lesions. In no case could the pus have been differentiated physically or bacteriologically from that encountered in chronic or severe abscesses of the lung.

It may thus be seen that *B. melaninogenicum*, while rather widely distributed, is closely associated with the presence of pathologic conditions and that, owing to its widespread presence in the mouth and more particularly in infected tonsils, it may readily be aspirated into the lungs under suitable conditions; there, in conjunction with other organisms, it may set up infection.

Of twenty-seven cases of abscess of the lung included in the present study, twenty-one were chronic, long-standing cases, and the material

was secured at or prior to operation. Of these twenty-one cases, a search for *B. melaninogenicum* was made in only seventeen, the other samples being studied before the presence of this organism was known; as a result the plates were discarded too soon to identify it. *B. melaninogenicum* was found in 94 per cent, or in sixteen of the seventeen recorded cases. In two of these cases, or in 9.5 per cent, the colonies of *B. melaninogenicum* on the plates constituted from 60 to 90 per cent of all the colonies present, and an exceedingly rapid breaking down of the hemoglobin took place (in less than forty-eight hours) with a concurrent production of an exceedingly foul odor, resembling that previously referred to. From one sample, or 5.9 per cent, between 20 and 30 per cent of all colonies growing were those of *B. melaninogenicum*. Five other samples, or 23.8 per cent, contained between 3 and 7 per cent of these organisms. Eight patients, or 38 per cent, had 2 per cent or less of the colonies, although numerically there were large numbers of the organisms present in the pus from most of these patients, and although from a casual inspection of the plates one might suppose them to be much more numerous. *B. melaninogenicum* was completely absent in only one case, or 5.9 per cent, even on repeated examination. The bacterial flora of this sample was quite different from that of any of the other samples studied, as may be seen by referring to case 2, table 1, which shows the bacteriologic observations in this sample.

In all of the samples of pus studied, there was a close relationship between the pus obtained from the patient and the bacterial flora in respect to *B. melaninogenicum*. This was particularly true in respect to the presence of granules. Of the samples of pus from typical chronic abscess of the lung in which granules were observed, *B. melaninogenicum* was found in all but one, as well as in many cases not included in this series. In the more putrid types of pus, in which the granules were often numerous, as compared with those found in less putrid types of pus, the numbers of *B. melaninogenicum* were always greatly increased. If only a few granules or none were present, there were only a few colonies of *B. melaninogenicum* found on culture. There was therefore a close relationship between the presence of these granules and the numbers of the black organisms present.

The odor given off from pus containing *B. melaninogenicum* is characteristic, and as the strength of the odor is apparently in direct proportion to the numbers of *B. melaninogenicum* present, an experienced worker may with considerable accuracy predict the absence or presence of the organism on this basis, together with the numbers to be expected. When grown on blood agar plates in symbiosis with fusiform bacilli, either alone or with streptococci, the organisms produce the same odor but in greater degree.

Results of Cultural Examination of Pus from Chronic Abscesses of the Lung

Case *	Sex	Anaerobic Growth †										Aerobic Growth †					Comment			
		Odor of Pus	Granules in Pus	Spirochetes in Pus	Identified			Unidentified				S Hemolyticus	Identified			Unidentified				
B Fusiformis	B Melanogenium				S Hemolyticus	S Viridans	Nonhemolytic Strep.	Other Organisms	Gram Positive Diplococci	Gram Negative Diplococci	Diphtheroids		Other Org in Pus	Nonhemolytic Strep	S Viridans	Nonhemolytic Strep	Pneumococci	Diphtheroids	Gram Positive Diplococci	Gram Negative Diplococci
1	M	Very foul	++++	+	7%	5%	—	22%	+	+	+	+	+	+	+	+	+	+	+	+
2	M	Slight	++	++	1 to 2%	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
3	M	Slight	—	—	4%	1 to 2%	—	+	+	+	+	+	+	+	+	+	+	+	+	+
4	M	Putrid	+++	+	5%	1%	—	4%	15%	45%	—	—	—	—	—	—	—	—	—	—
5	M	Foul	+++	+	1%	1%	—	+	+	30%	—	—	—	—	—	—	—	—	—	—
6	F	None	+++	0	<1%	25 to 30%	—	60 to 75%	+	—	—	—	—	—	—	—	—	—	—	—
7	M	Slight bloody	+	+	1%	<1%	—	—	+	60 and 10%	—	—	—	—	—	—	—	—	—	—
8	F	None	++	—	3%	1%	+	—	+++	40%	—	—	—	—	—	—	—	—	—	—
9	M	Slight	—	0	1 to 2%	7%	—	5 to 10%	+++	40%	—	—	—	—	—	—	—	—	—	—

The mere presence or absence of an organism in a pathologic lesion cannot, of course, be taken as a criterion as to its etiologic significance in connection with that lesion, and while there are no exact experimental data as to the relationship between *B. melaninogenicum* and abscesses of the lung, certain factors would seem to show that it may be of great importance in this disease. The organism may be present, of course, only as a secondary invader or saprophyte and may grow more readily in the older lesions simply because of better conditions of nutrition. Experimental evidence is against the idea of any one organism causing these lesions, but rather points to several organisms growing in intimate symbiosis with each other as giving rise to the condition; one organism, enabled to grow by means of the withdrawal and continual exclusion of oxygen by the other bacteria, penetrating into healthy tissue, injuring it so that other organisms of the group may follow and injure it still further, allowing those organisms which live on necrotic or liquefied tissue to complete the process. The most frequently found and probably the chief organisms concerned in this process are *B. melaninogenicum*, fusiform bacilli, spirochetes and streptococci, especially of the viridans type. In pure culture, *B. melaninogenicum* so far has proved to be devoid of pathogenic properties, but in symbiotic growth its numbers increase rapidly in experimental lesions, coincident with a marked change in the character of the pus from the light yellow pus seen in early lesions, which is largely devoid of odor, to the chocolate-brown, foul smelling pus seen in the advanced cases in human beings. In the series of experiments by Allen¹ on the experimental production of abscesses of the lung in dogs, pus from one of the patients studied in this series (case 21) was secured at operation, kept at 37 C., and introduced into the bronchus of a dog under ether anesthesia, following which the bronchus was ligated. After twenty-six days the dog, in a dying condition, was chloroformed; autopsy disclosed an extensive abscess in which was found a large amount of foul smelling, dark brown pus which physically resembled that originally introduced, except that it was slightly more liquid, and which had a strong odor of *B. melaninogenicum*. A large number of cheesy granules was found in the pus. However, while only about 1 per cent of colonies of *B. melaninogenicum* was found in the original pus, in the pus from the dog the anaerobic growth showed approximately 50 per cent of the organisms from one sample and almost 100 per cent from another to be *B. melaninogenicum*, no sample showing less than 50 per cent of the organisms. Aerobically, practically 100 per cent of the colonies growing were of a small, non-hemolytic streptococcus. The soft, yellowish, cheesy granules were found in large numbers, and varied in size from a fraction of a millime-

ter to several millimeters in diameter. On staining, these granules were seen to teem with spirochetes, and with considerable numbers of fusiform bacilli. Few spirochetes were found in the liquid pus. The hemoglobin in the blood agar plates was destroyed rapidly, the plates all becoming decolorized in less than four days, coincident with the formation of an intense black pigment in the colonies of *B. melaninogenicum*. Numerically, the fusiform bacilli were present in considerable numbers, but relatively there was only a small percentage of such colonies present. The same gram-positive streptococcus seen in the aerobic cultures appeared in the anaerobic cultures, but in much smaller numbers.

It may be seen that in this experimental abscess, the numbers of *B. melaninogenicum* increased tremendously. The other organisms, while still numerically present in large numbers, were greatly decreased in percentage at the expense of *B. melaninogenicum*. Results similar to those secured in this experiment were obtained a second time, using another patient (case 19) and another experimental animal.

While the results of only one or two experiments can at best be merely indicative, the evidence is at least suggestive that *B. melaninogenicum* may and probably does play more than a passive rôle in the production of abscesses of the lung. It should be repeated, however, that it is unlikely that any one organism may be incriminated as the etiologic agent, but rather that several organisms, as previously mentioned, act symbiotically to bring about this condition. The spirochetes and fusiform bacilli are the outposts of the advancing infection, producing an injury which is carried on to completion by streptococci and *B. melaninogenicum*. The streptococci as well as other aerobic cocci are of aid in this process not only because of their inherent pathogenic powers, but also because of their ability to maintain anaerobic conditions, an essential for the other organisms. To the presence of *B. melaninogenicum* must also be attributed much of the disagreeable nature of the infection, because of the foul nature of the pus so produced.

Of the six cases studied in which operation was performed, the presence of *B. melaninogenicum* was recorded in only three, and here only in small numbers. However, since the pus from these patients was obtained by swabbing from the exterior through the wound fissure, there was less chance for an anaerobic flora than in the cases in which no operation was performed. Even with deep swabbing, however, few colonies of *B. melaninogenicum* were ever found. There is a definite decrease in these organisms following operation; this decrease is both quantitative and, more especially, qualitative, there being a great increase in aerobes at the expense of the anaerobes.

BACILLUS FUSIFORMIS

Of the twenty-one cases studied in which no operation was performed, *B. fusiformis* was found in twenty cases, or 95 per cent, by microscopic examination. By means of cultural tests, the organisms were found in twenty-one, or 100 per cent, of the cases. It is of interest to note that in several cases microscopic examination showed the presence of myriads of gram-negative organisms, with a few scattered gram-positive organisms of the same type, which were at first diagnosed as typical *B. fusiformis*, but which on culture proved to be gram-positive diphtheroids, which have the same size and shape as *B. fusiformis*. Even an experienced observer, therefore, finds it unsafe to trust mere microscopic examination in establishing the presence or numbers of *B. fusiformis* in the lesions. In the cases mentioned, actually only a few colonies of *B. fusiformis* developed, although large numbers of the diphtheroids were found. Cases were also encountered in which a large number of organisms which appeared to be vibrios was found, but which on culture proved to be *B. fusiformis*.

In only three, or 14.3 per cent, of these twenty-one cases were the colonies of *B. fusiformis* present in a concentration of from 50 to 60 per cent or in the majority. In one case, or 4.75 per cent, 25 per cent of the organisms cultivated were *B. fusiformis*. In four cases, or 19 per cent, between 5 and 7 per cent of the colonies were those of *B. fusiformis*. In the other cases, numbering thirteen, or 62 per cent, from 1 to 4 per cent of the colonies were those of *B. fusiformis*. As in the case of *B. melaninogenicum*, in enumerating these organisms one should actually count the various colonies found in order to arrive at any accurate estimate as to the percentage of various types of bacteria present, as it is easy to overestimate the percentage of an organism which has so characteristic and striking a colony as *B. fusiformis*.

Several different types of *B. fusiformis* were found in these lesions, the most numerous of which were the types I and II previously described by me.⁸ Type IV is frequently seen microscopically in small numbers in the pus, but due to difficulties in cultivation, it is very hard to grow and count it in numbers corresponding to those present in the lesion.

In two of the six cases in which operation was performed, no fusiform bacilli were found by microscopic examination or by culture. One case, microscopically negative, was positive by culture. One case, weakly positive microscopically, was weakly positive by culture, colonies of *B. fusiformis* constituting about 0.1 per cent of the total flora. Two

8. Varney, Philip L.: The Serological Classification of Fusiform Bacilli, *J. Bact.* **13**:275, 1927.

cases that were weakly positive microscopically revealed on cultivation considerable numbers of fusiform bacilli. Of the six cases in which operation was performed, therefore, fusiform bacilli were found in four, and were absent in two. As in the case of *B. melaninogenicum*, the number of these organisms in patients undergoing operation was found to be greatly decreased. In general, the microscopic method for the detection of fusiform bacilli has proved to be less reliable and sensitive than the cultural test, contrary to general opinion.

SPIROCHETES

In only one of the twenty-one cases in which operation was performed was there apparently a greater number of spirochetes than of other organisms in the microscopic preparations. Since the relative numbers of these organisms can be determined only by comparatively unreliable microscopic methods, the numbers actually present cannot be checked by cultural controls. In two additional cases spirochetes were found in large numbers in the lesions, and in three cases in fairly large numbers. In eight cases, or 38 per cent, spirochetes were present in numbers corresponding to between one and five per field. In six samples no spirochetes were found. Of the twenty-one cases, therefore, spirochetes were present in 71.4 per cent and absent in 28.6 per cent.

Of the cases in which operation was performed, spirochetes were found in only two, and here were present in small numbers; one of these cases showed only one spirochete to each two fields examined, and the other, approximately one or two organisms per field. The other four cases were entirely negative even after long search. It is difficult, however, to search for spirochetes in pus from an organizing wound, as the large amount of fibrin and cellular debris makes it almost impossible to stain the organisms and not stain the background to such an extent that the organisms are concealed. It may safely be said, however, that there is an almost total absence of spirochetes in the patients operated on.

STREPTOCOCCI

In only three of the twenty-one cases in which operation was not performed were colonies of *Streptococcus hemolyticus* found in numbers greater than a few per plate under anaerobic cultivation; in these cases they constituted from 6 to 7 per cent of the total flora. In practically all the cases a few colonies were found on the plates, but in too small a number to be recorded.

In five of the twenty-one cases, *Streptococcus viridans* was found, in anaerobic cultures, to constitute a majority of the organisms present, varying from 50 to over 80 per cent of the total number of colonies

present. In five other cases they were found in smaller numbers, and in eleven remaining cases they were found in very small numbers.

In the aerobic cultures the numbers of streptococci were greatly increased over those cultured from the same material but incubated under anaerobic conditions. In four cases, *S. hemolyticus* constituted a majority of the flora, occurring in as great a concentration as from 90 to 98 per cent. In three other cases they were found in large numbers, varying from 10 to 20 per cent, and in five other cases they were found in only small numbers, constituting from 1 to 5 per cent of the flora.

Under aerobic conditions, *S. viridans* was frequently found in large numbers, as well as constituting a high percentage of the total flora present; colonies of this organism constituted a majority of the flora in seven cases, the percentage varying from 60 to 100 per cent. The liquid portions of the pus ordinarily contained larger numbers of the streptococci than the granules. In six cases, from 22 to 40 per cent of the colonies growing were those of *S. viridans*. In four cases they were found in small numbers varying from 1 to 5 per cent of the total flora, and in the remaining cases, they constituted only a negligible part of the flora, only an occasional colony being found out of thousands present. Thus, of twenty-one cases in which there had been no previous treatment, eighteen, or 85.7 per cent, were positive for *S. viridans*.

Of the six cases studied in which treatment was given, four showed a high percentage of *S. hemolyticus*, the percentage varying from 50 to 99, under anaerobic conditions. Under aerobic cultivation, only one of these cases showed a majority of this organism present, and in only two of the six cases were colonies of *S. hemolyticus* encountered. In all of the treated patients there was a sharp decrease in the number of organisms of all kinds, with an increase in percentage of *S. hemolyticus* over that encountered in the untreated patients. In contrast to the apparent increase in the numbers of *S. hemolyticus* there was a total lack of colonies of *S. viridans* on any of the anaerobic plates, and in only one of the cases was this organism found on the aerobic plates.

Small gram-negative and gram-positive cocci were encountered in many of the samples examined, the gram-negative organisms outnumbering the gram-positive forms. These organisms were of several different species, and apparently had no constant relationship to the material under study.

In the table, no attempt was made to include the many organisms that were found, chiefly in small numbers, in only one or two of the samples studied, and that were probably saprophytic or derived from accidental contaminations from the sputum.

In only two cases were pneumococci found in large numbers. In one case they constituted 20 per cent of the flora, and in another they were present in a concentration of 95 per cent under aerobic conditions. In the first case, the pneumococci were accompanied by hemolytic *Staphylococcus aureus* which constituted 42 per cent of the flora. Staphylococci were rarely encountered in this series of cases.

CONCLUSIONS

Twenty-seven cases of chronic abscesses of the lung were studied in respect to their bacterial flora, twenty-one of which were from previously untreated patients. Streptococci, fusiform bacilli, *B. melaninogenicum* and spirochetes were the organisms most commonly encountered in the material from the lesions of the untreated patients; *S. viridans* was found more frequently than *S. hemolyticus*. In the treated patients, the fusiform bacilli, spirochetes and *B. melaninogenicum* greatly decreased in number or disappeared altogether, coincident with a relative increase of *S. hemolyticus*. The bacterial flora of material from chronic abscesses of the lung showed a remarkable similarity to that from infected tonsils, cervical abscesses and diseased teeth and mucous membranes.

7. EARLY CARCINOMA OF THE LUNG*

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It is generally recognized that considerable light will be thrown on the histogenesis of cancer, especially that of internal organs, through the study of early cases, and through the study of inflammatory or other irritative processes that may produce excessive epithelial proliferation. Much that would increase the knowledge of carcinoma of the lung was hoped for after the influenza epidemic of 1919 and 1920. One is struck, however, by the fact that although innumerable pathologic reports have been published on influenza, only a few mention excessive regeneration of the epithelium of the lung that may possibly be interpreted as significant in the etiology of carcinoma. Askanazy,¹ Glaus and Fritsche,² Winternitz and others,³ Wolbach and Frothingham⁴ and Schmidtmann⁵ have described epithelial proliferation that appears to begin in the bronchus and may invade the alveoli and in some instances the peribronchiolar tissue. Most of the cases described were found in people who died soon after the onset of the disease. In his recent review of this subject, Weller⁶ stated that not influenza itself but "the sequelae of influenza, so far as they bring about bronchiectasis or chronic fibroid pneumonia are of importance" as precursors of carcinoma. The latter pathologic changes may play a rôle irrespective of the organism or mechanism that produces them. As early as 1876, Friedländer⁷ discussed this relation between certain pathologic conditions of the lung and carcinoma.

Chemical and physical irritants have also been emphasized as important factors in human and experimental carcinoma of the lung. This phase of the problem also is reviewed by Weller.

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1. Askanazy, M.: Cor.-Bl. f. Schweiz. Ärzte 49:465, 1919.

2. Glaus, A., and Fritsche: Cor.-Bl. f. Schweiz. Ärzte 49:72, 1919.

3. Winternitz, M. C.; Wason, I. M., and McNamara, F. P.: The Pathology of Influenza, New Haven, Yale University Press, 1920, pp. 61.

4. Wolbach, S. B., and Frothingham, C.: Influenza Epidemic at Camp Devens in 1918, Arch. Int. Med. 32:571 (Oct.) 1923.

5. Schmidtmann, M.: Virchows Arch. f. path. Anat. 228:44, 1920.

6. Weller, C. V.: Pathology of Primary Carcinoma of Lung, Arch. Path. 7: 478 (March) 1929.

7. Friedländer, C.: Virchows Arch. f. path. Anat. 68:325, 1876.

The histologic picture of the lung in the case that we are about to describe has a few points in common with that recorded in some of the conditions just mentioned. However, the impossibility of finding any clinical relationship between the two and the fact that the changes in this lung are so much more advanced than those described in the other conditions leave us with no doubt but that we are dealing with an early carcinoma of the lung and not with a benign epithelial hyperplasia. Our study was brought about through an accidental observation in the routine microscopic study of a case that had given no clinical or gross anatomic evidence of any unusual pulmonary change. The relatively slight and

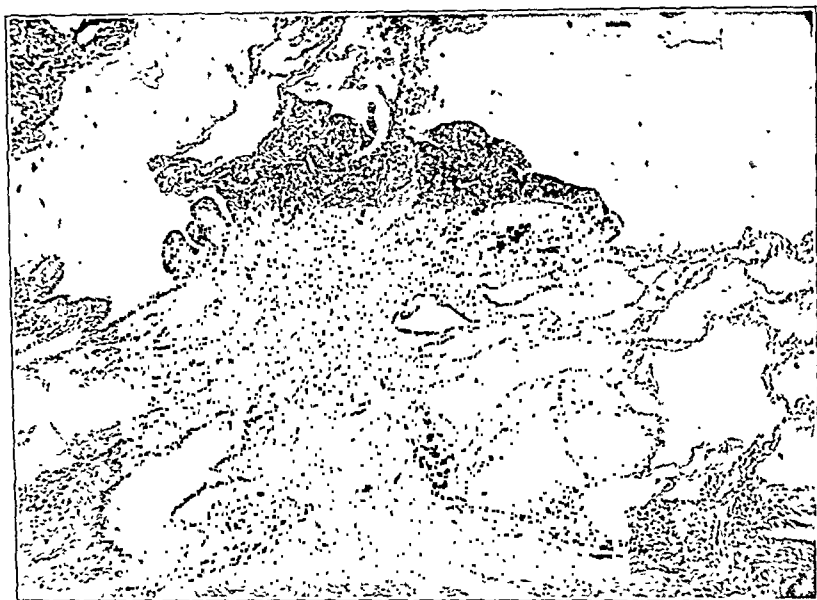


Fig. 1.—Papillomatous hyperplasia of the epithelium of the ductus alveolaris. Hematoxylin and eosin; $\times 61$.

early involvement offers valuable information concerning the histogenesis of multiple carcinoma of the lung.

E. N., a colored woman, aged 78, entered the surgical service at Barnes Hospital suffering from a fracture of the right femur, sustained in a fall from a porch. She was mentally clear and alert. During her stay of one month in the hospital, there was ample time for obtaining a history. She said that she had never been sick, except for some vague diseases of childhood. We can be reasonably sure that she had had no illness for ten years at least. Except for the condition of the lung, there was nothing of interest in the physical or postmortem examination.

Grossly, the lungs were pale pinkish gray, mottled with black. In the right upper lobe the pleura was somewhat thickened, and on section there appeared to be an increase in connective tissue and coal pigment. At the apex, there was a minute calcified nodule. Because the changes were apparently slight, the whole lungs were not preserved.

After an early carcinoma had been discovered microscopically, all the blocks of tissue that had been preserved in solution of formaldehyde and alcohol were cut serially. The sections of lung tissue showed a moderate, fairly diffuse fibrosis (figs. 1 and 5), with small amounts of carbon particles embedded in the meshes of the connective tissue. In no place did the fibrosis suggest healed tubercles, but this did not absolutely rule out an old tuberculous process. The smaller bronchi were dilated, and their walls only slightly infiltrated with lymphocytes. The bronchioles and ducti alveolares were markedly dilated and irregular, with hypertrophic epithelium. Small collections of lymphocytes and occasional plasma cells were found here and there in the lung. Many of the alveoli were emphysematous. Three small cancer masses were found, which were distinct and separate from one another.

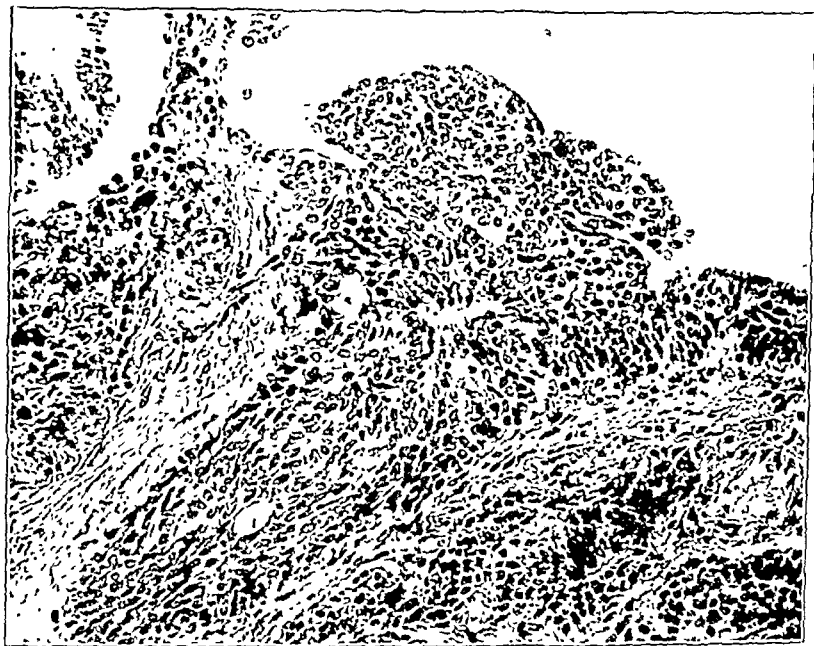


Fig. 2.—High power magnification of figure 1, showing the appearance of the cells. Hematoxylin and eosin; $\times 244$.

Figures 1, 2, 3 and 4 are photographs from one of the tiny cancer nodules. Figure 1 shows a marked hyperplasia, papillomatous in appearance, of a ductus alveolaris. To the left, one can see the transition between the unusually tall one-celled epithelial lining of the ductus alveolaris and the many-celled neoplastic tissue; to the right the tumor is seen in communication with emphysematous alveoli. Figure 3 gives a higher power photograph of this transition. In the lower left corner of figure 1 are a dilated terminal bronchiole and a ductus alveolaris. In the right center are two ducti alveolares in communication with alveoli. A little above the center, the tumor extends into and lines an alveolus. The tumor cells can be studied better in figure 2. They are of medium size, with light staining nuclei; nearer the base they are elongated, while at the surface the cells assume a polygonal shape.

Invasion of the lymphatics evidently occurs early; for this tumor, which is less than a millimeter at its widest, shows definite invasion of the lymphatics. Figure 4

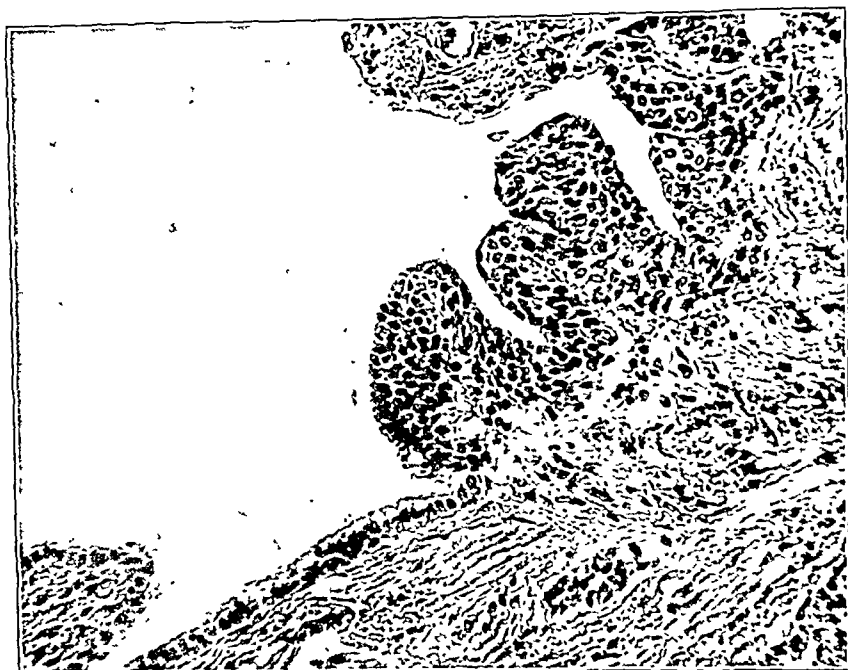


Fig. 3.—Transition between hypertrophic epithelium of the ductus alveolaris and the papillomatous new growth. Hematoxylin and eosin; $\times 269$.

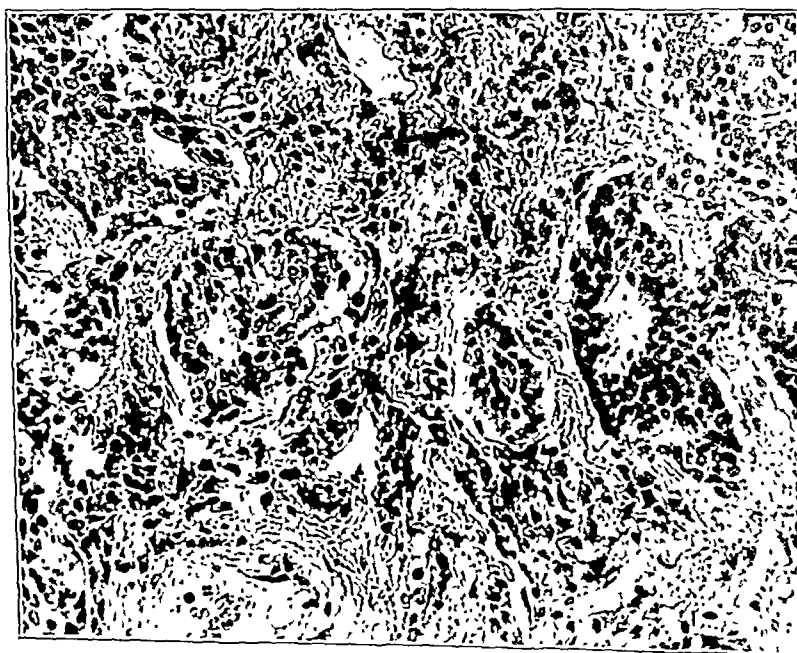


Fig. 4.—Another part of the same tumor, showing invasion of the lymphatics. Hematoxylin and eosin; $\times 294$.

is a photomicrograph of another area from the same tumor nodule showing small nests of cells in lymphatics. The cells show some irregularity in size and in shape, with nuclei which stain somewhat deeper than those previously described.

Figures 5, 6 and 7 picture the second tiny tumor. Figure 5 is a low power photomicrograph of the entire tumor mass, which consists of small islands of tissue lying in lymphatics. Figure 6, which is a high power photograph of the right upper corner of figure 5, is the only area in which there is a possible connection with an epithelial surface. The layer of cells along the right upper margin of the tissue might be taken for epithelium lining a ductus alveolaris, especially since in figure 5 the tissue lies at the opening of a distended alveolus. Unfortunately, all the tumor had been cut away when the routine sections were made so that serial sections of what remained of the block gave no further information. Figure 7 is a high power view of one group of cancer cells in a lymphatic, in

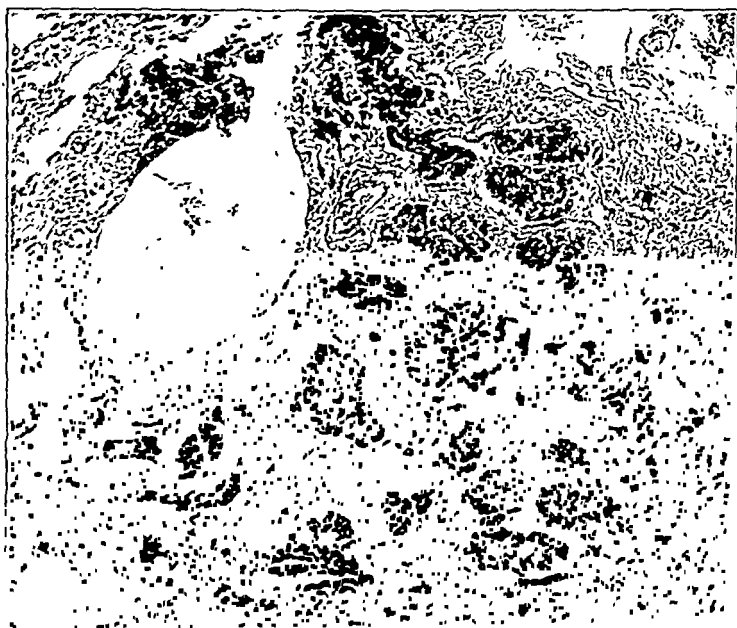


Fig. 5.—Photomicrograph of second small neoplasm. Most of the cancer is seen in lymphatics. Hematoxylin and eosin; $\times 111$.

which one may see two questionable mitotic figures, and some variation in size, shape and staining quality of the cells.

Although the third nodule was sectioned completely, no definite primary site could be detected unless figure 8 were interpreted as such. However, this is probably cancer tissue growing into an alveolus. In figures 9 and 10 taken from the third nodule, differentiation of the invading tumor is apparent; in figure 9, a solid sheet of cells is seen in one lymphatic, and a pseudo-alveolar arrangement in another; in figure 10, flat elongated cells are found in a lymphatic. The blood vessels were not invaded by the cancer.

The other organs did not show any change which might be connected with the process found in the lung; no evidence of carcinoma was found in any other part of the body.

COMMENT

One of the most interesting features of this early neoplasm is the origin of cancer of the lung from the ductus alveolaris. The bronchi and bronchial glands have been accepted as definite sites of origin for cancer. The alveolar epithelium has been a doubtful source, although Ewing⁸ has accepted it in his classification. We could find no reference to the ductus alveolaris as a primary site. In view of this uncertain alveolar origin of cancer, especially since Fried⁹ and Rose¹⁰ in their recent work have again seriously questioned an epithelial lining of the



Fig. 6.—Possible point of origin of second tumor from a ductus alveolaris. Hematoxylin and eosin; $\times 524$.

alveoli, we think that it would be of value to restudy the cancers to trace a possible origin from the ductus alveolaris. This is especially true of the multiple nodular carcinomas, which the case that is being presented resembles.

If we had been more fortunate in the amount of tissue that had been preserved, we could have answered definitely the question as to the

8. Ewing, J.: *Neoplastic Diseases*, Philadelphia, W. B. Saunders Company, 1928.

9. Fried, B. M.: *Origin of Histiocytes in Lungs*, *Arch. Path.* **3**:751 (May) 1927.

10. Rose, S. B.: *Finer Structure of the Lung*, *Arch. Path.* **6**:38 (July) 1928.

multicentric origin of pulmonary carcinoma. There can be no doubt about the primary site in tumor 1. Although we think that figure 6 shows a probable primary site in tumor 2, we cannot say so with certainty. Tumor 3 is metastatic. The studies that have been made on this type of carcinoma of the lung favor a multicentric origin. Multiple cancers of the lung, however, may be produced in a way other than from multiple primary sites. The early invasion of lymphatics sends numerous small nests of cells to other parts of the lung. In a lung in which there has been an old inflammatory lesion that has resulted in scarring, a large number of the lymphatics are blocked. The cancer metastases thus can-

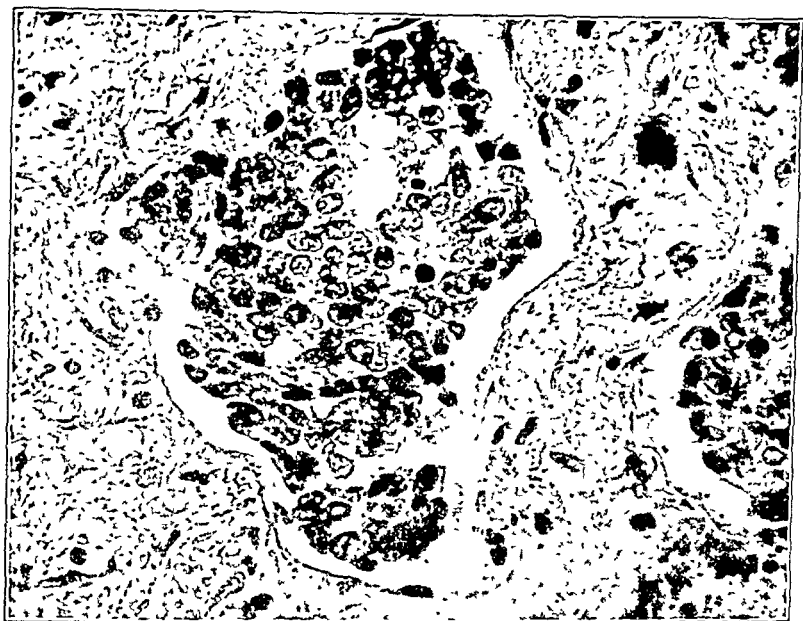


Fig. 7.—A higher power magnification of figure 5 of the cancer tissue in a lymphatic. Hematoxylin and eosin; $\times 536$.

not proceed beyond the scar and grow in the region of this fibrosis. The neoplastic tissue can travel by retrograde metastases to other parts of the lung and there set up small cancer nodules. In the three small tumors, there was little difference in their size, even though one of them is probably a metastasis, thus denoting early invasion of the lymphatics and dissemination to other parts of the lung. It is even possible for the tumor metastases to get to the other lung by way of retrograde growth from tracheobronchial lymph nodes where the lymphatics of both lungs meet. This may be a more plausible way, if the tracheobronchial lymph nodes have been the site of a chronic inflammatory process. Two sources must therefore be considered to account for multiple nodular carcinomas of the lung: multicentric origins and early metastases.

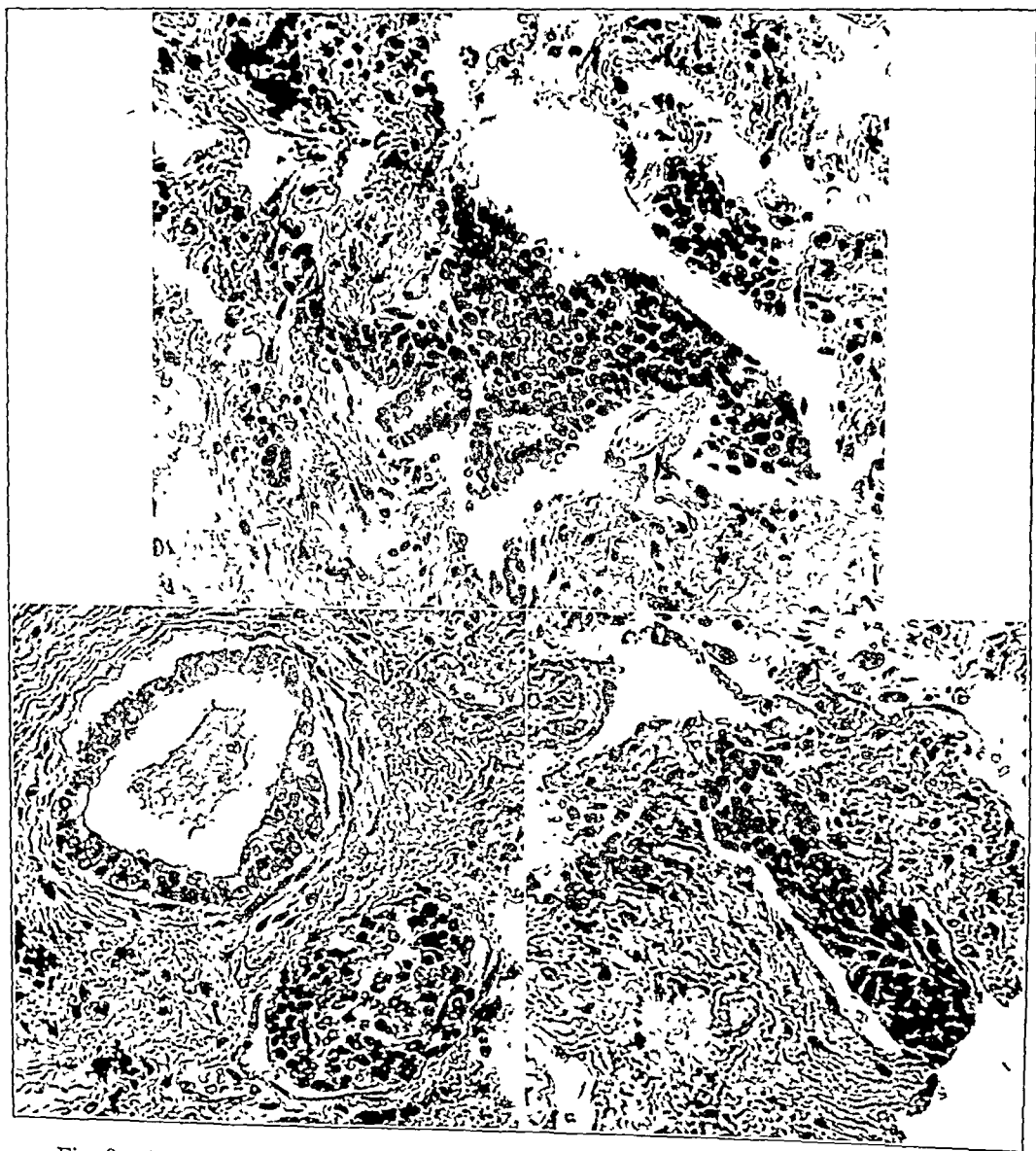


Fig. 8.—Areas from the third tumor nodule, showing invasion of alveoli and lymphatics. Notice the variety of forms the tumor may assume. Hematoxylin and eosin; $\times 300$.

Tumors 2 and 3 appear to be the most actively growing. The invasion of the lymphatics is extensive. The nuclei stain deeply, and the cells vary in size and in shape. Figure 8 shows the marked differences in appearance that cancer tissue may assume at an early stage, when the new growth is as yet microscopic in size. Few questionable mitoses were seen in any of the sections.

The question of the relationship of this process to other processes that produce epithelial proliferation may be briefly discussed. The experimentally produced proliferation of the lung parenchyma such as that produced by Winternitz, Smith and McNamara¹¹ by tracheal insufflation obviously plays no rôle in this case.

We have mentioned the reported occurrences of epithelial proliferation that have been observed in influenza, with which the condition in our case may be confused. No history of influenza was obtained, nor was there any history of infection of the lungs, although, to make allowances for the age of the patient and the possibility of poor memory, we have limited ourselves arbitrarily to ten years as the period during which we can be reasonably sure that there was no infection. We have been unable to find the report of any case with a histologic picture similar to the one described in which any relationship to influenza could be determined. The presence of connective tissue and the dilatation of the bronchioles may denote a previous inflammatory or irritative process; still, we have no means of determining the nature of that process.

At Barnes Hospital, although many postmortem examinations have been performed on people who have had influenza, nothing resembling this change in the lung has been found. In a personal communication, Dr. MacCallum stated that he has had a similar experience at Johns Hopkins Hospital. It would be difficult to imagine the existence of this lesion for a period of many years, as one would have to suppose if the patient had had influenza at some earlier period. Furthermore, if there had been a history of influenza, the inclination would still be great to look on this process as an early carcinoma, especially since one of these tumors in serial sections showed no relationship to an epithelial surface, and also because of the extensive invasion of the lymphatics and the marked differentiation of the epithelial nests.

CONCLUSIONS

1. An early primary carcinoma of the lung is described.
2. The epithelium of the ductus alveolaris is found to be the primary site.
3. Evidence is presented to show that multiple nodular carcinomas of the lung may arise from both multiple origins and early metastases.

11. Winternitz, M. C.; Smith, G. H., and McNamara, F. P.: *J. Exper. Med.* 32:205, 1920.

8. CONSEQUENCES OF VARIATIONS IN MEDIASTINAL PRESSURE; MEDIASTINAL AND SUBCUTANEOUS EMPHYSEMA *

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The following experiences and observations concern the effect of variations in mediastinal pressure in the experimental animal. Particular attention has been paid to some of the consequences of mediastinal emphysema.

We use the term "increased mediastinal pressure," as did Jehn and Nissen,¹ in the same sense as "increased intracranial pressure."

Irrespective of the mechanism, any serious encroachment on the mediastinum must of necessity produce changes which are either local or general. Such changes may vary and may be dependent on the normal arrangement of the anatomic structures in the region concerned and their resistance to stresses and strains. It is certain that in a closed thorax one structure cannot expand to any great extent except at the expense of another. Air can, of course, escape into the subcutaneous tissues through the jugulum or dissect along fascial planes.

Graham² has shown that the presence of a liquid, gas or tumor in the pleural space may disturb the intrapleural pressures. Although all of these will exercise pressure on the lung, each operates in a slightly different manner, liquids acting in accordance with the laws of hydrostatic pressure, gases in the absence of adhesions exerting an equal pressure throughout, and tumors exerting their chief pressure wherever they happen to be located. Similar substances occupying the mediastinum act in practically the same way. Graham³ has also shown that in unilateral open pneumothorax the important matter is the amount of air which enters through the opening at each inspiration and the ability of the individual to compensate for the encroachment on his respiratory

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1. Jehn, W., and Nissen, R.: *Pathologie und Klinik des Mediastinalempysemes*, Deutsche Ztschr. f. Chir. **206**:221, 1927.

2. Graham, E. A.: The Importance of the Vital Capacity in Thoracic Surgery, J. A. M. A. **75**:992 (Oct. 9) 1920.

3. Graham, E. A.: Alterations of Intrapleural Pressure and Their Significance, *Medicine* **3**:417, 1924; A Reconsideration of the Question of the Effects of an Open Pneumothorax, *Arch. Surg.* **8**:345 (Jan.) 1924.

surface which is caused by the open pneumothorax. The same may be said of mediastinal emphysema with the exception that the important factor in this case is the amount of air retained in the mediastinum. The retained air is inspired air which cannot be expired. The position and size of the opening which is allowing the air to escape into the mediastinum is therefore of some import. Granted that air does not escape into the subcutaneous tissue or that a pneumothorax does not develop, the acting mechanism will then be quite similar to that of an uncomplicated valvular pneumothorax. Also of considerable importance, therefore, is the pathway which the escaped air takes.

The normal pressure on the mediastinal structures has been roughly expressed as being that of atmospheric pressure minus the pressure exerted during the normal retraction of the lung (Assmann⁴).

We have tried in a general way to consider the consequences of variations in mediastinal pressure from the standpoint of those expressive of either inspiratory or expiratory (dyspnea) distress. Attention has been paid to the effects of variations in mediastinal pressure on the great vessels. For it soon became evident that they may be readily compressed and the respiratory passages remain free as in cases of the so-called status thymico-lymphaticus. Anatomically considered, it is much easier for compression of the large blood vessels to occur than of the trachea or bronchi. Cyanosis and dyspnea were more often observed to be expressions of compression of the former than of the latter. Pulmonary compression and mechanically impaired heart action are considerations which demand considerable attention. For the resultant emphysema which may be patchy, unilateral hypoventilation of one lung, hyperventilation of the other and the stagnation of blood in the lungs which in some measure is also due to hindered heart action may soon apparently lead to edema of the lungs and to the development of fluid in the pericardial cavity. The vital capacity can thus be quickly reduced.

Edema of the tracheobronchial mucous membrane is, of course, another consideration. Such factors as carbon dioxide tension, hydrogen ion concentration and vagus regulation have received but scant attention. It is, however, appreciated that they must play a significant rôle in the experiments here recorded.

We have recorded some of the variations in the arterial, venous and intrapleural pressures which result from changes in the size, shape and contour of the anterior and posterior mediastina. Changes noted in the respirations were also recorded.

The results of our experimentation perhaps permit us to make some few clinical analogies throughout our discourse.

4. Assmann, H.: *Klinische Roentgen diagnostik der inneren Erkrankungen*. Leipzig, F. C. W. Vogel, 1929.

HISTOLOGY OF THE MEDIASTINUM

The finer histologic structure of the mediastinum has recently received consideration at the hands of Seifert.⁵ He has shown definitely that there is a histologic basis for the reason why the mediastina of various animals react differently to artificial pneumothorax. He noted that the histologic structure of the mediastinum is in some measure dependent on the age of the animal and that the mediastinum in the dog resembles in the anatomic sense the greater omentum of the dog. He added, however, that it is not possible to determine on a purely histologic basis as to whether the function of both can be considered the same. Seifert showed, as is well known, that the mediastinum drains the pleura. Herrfarth⁶ and others have pointed out that the pleural cavity drains readily to the mediastinum. We found that if india ink were injected into the neck it soon made its way to the mediastinum. When injected substernally above the level of the hilum of the lung, it soon found its way into the lung. When we injected india ink under the lower portion of the sternum it was observed after several weeks on the pericardium and pleura and in the mediastinum. But few ink particles were to be noted in the lungs.

The mediastinum also apparently contains cells which have phagocytic properties. The mediastinum of the rabbit has been found to be histologically and experimentally a denser and more resistant structure than that of other experimental animals. Between the pericardium and diaphragm, where the mediastinum surrounds the so-called bursa infracardiaca, the mediastinal pleura of the rabbit is made up of little fat nodules and fat conglomerate structures which resemble the similar bodies found in the greater omentum of the rabbit.

The mediastinal pleura of the human adult is denser and thicker than that of the child and than the analogous membranes of the various experimental animals. The mediastinal pleurae of the rabbit and monkey, Seifert stated, do not resemble the greater omentum in the same way as the mediastinal pleura of the dog which in this respect closely resembles that of man.

TECHNIC

Practically all our experiments were performed on rabbits, because the mediastinum of the rabbit is best fitted to stand stresses and strains—more so than other animals which would be suitable for such experimentations.

The arterial pressure was recorded by means of a cannula which had been introduced into the carotid artery and connected up with a mercury manometer. The venous pressure in the jugular vein was recorded by means of a water

5. Seifert, E.: Ueber den feineren Bau des Mediastinum, Arch. f. klin. Chir. **151**:237, 1928.

6. Herrfarth, E.: Beitrag zur Infektiösität der Pleura, Zentralbl. f. Chir. **41**:2582, 1928.

manometer which was fitted up with a cork rider and a very fine, thin-bored, glass recording arm. A glass tube was introduced into the trachea and recorded respirations on a tambour while the intrapleural and mediastinal pressures were recorded on two pneumothorax apparatus. Other details with regard to the technic of the experiments will be noted under the experiments which they concern.

The use of the pneumothorax apparatus together with the taking of roentgenograms at intervals and injections of iodized poppy seed oil 40 per cent performed at the end of the experiments in most instances enabled us to observe the presence or absence of a pneumothorax and quite often permitted us to recognize when a pneumothorax had developed. For although the development of a pneumothorax is often due to faulty technic, there are other occasions when it obviously means only that the increased mediastinal pressure was greater than the mediastinum could withstand.

ANATOMY OF THE MEDIASTINUM

The weak points of the mediastinum are under the sternum, where the thymus normally lies and behind the heart where both mediastinal pleurae come in contact. Two triangles are thus formed, the uppermost *one having its apex where the heart begins and the lowermost one having its apex take off from the apex of the uppermost*. The anatomic arrangement of the mediastinum, therefore, predisposes to the localization of fluids which collect in the mediastinum. But they do not become encapsulated. The resorptive powers of the mediastinum are greater than those of the pleural cavities or of the abdominal cavity.

It is perhaps best to consider that the mediastinum consists of an anterior and posterior compartment. The anterior mediastinum is made up of the so-called trigonum thymicum (mediastinum supracardiacum) and of the triangle occupied by the heart and great vessels. The anterior mediastinum, therefore, lies in front of the root of the lung, the posterior mediastinum behind the root of the lung.

In the mediastinum supracardiacum the first layer that one meets directly under the sternum is loose fatty tissue, which is, in man, for the most part, the remains of the thymus gland. Willis⁷ has shown that the tracheobronchial lymph nodes of the rabbit are small but that the thymus is extremely large. The second layer is formed by the innominate veins and by the inferior thyroid veins and the internal mammary veins, both of which empty into the first mentioned veins. The next structure which is met and which lies for the most part in the mid-line is the superior vena cava. It is well to remember that the lower half of the superior vena cava is covered by pericardium and is therefore not visible. The great vessels in reality pierce the pericardium. The third layer is composed of the arch of the aorta and the branches which it gives off. The posterior portion of the third layer and the fourth

7. Willis, H. S.: Studies on Tuberculosis Infection, Tracheo-Bronchial Lymph Nodes of Rabbits and Their Blood Supply, *Am. Rev. Tuberc.* 14:237, 1926.

layer composed of the trachea and the esophagus form the anterior wall of the posterior mediastinum. Other structures to be considered in the posterior mediastinum are the sympathetic nerves, the recurrent laryngeal nerves and lymph glands. The attachments of the diaphragm, the cardiophrenic angles and particularly the relationship of the various structures which leave the mediastinum and perforate the diaphragm are of extreme importance when considering the consequences of increased intramediastinal pressure. The foregoing descriptions concern in general the anatomy of man, but the anatomy of the rabbit in this region differs in no essential practical manner.

Under the mediastinal pleura, on either side of the mediastinum supracardiacum, lie the phrenic nerves and medial to them both the vagi, cardiac depressor and other nerves.

EXPERIMENTS WITH RUBBER BALLOON IN MEDIASTINUM

These experiments illustrate the effects of sudden confined increase in mediastinal content and pressure and how these effects can be made to disappear just as readily as they came by reducing the confined pressure, provided, of course, that the increased pressure is not kept up too long or the procedure repeated too often. The consequences, which were local and general, varied directly with the extent to which the balloon had been inflated and the position which it occupied in the mediastinum.

The usual technic was observed in these experiments. A little rubber balloon was attached to either a glass or rubber tube and connected up with a syringe or pneumothorax box and placed in the mediastinum.

EXPERIMENT 1.—The left intrapleural pressure was -8 , and the right intrapleural pressure -10 , 0 . The mere taking of pneumothorax readings sometimes caused a slight temporary drop in blood pressure. Fifty cubic centimeters of air was injected into the balloon. Part of this air occupied the dead space in the glass tube. The left intrapleural pressure then became -14 , and the right intrapleural pressure -4 . An additional 50 cc. of air was then injected, and a roentgenogram showed no evidence of pneumothorax. The intramediastinal pressure was now sufficient to compress both the carotid artery and the trachea so that they were recorded on the tracing as straight lines.

EXPERIMENT 2.—The right intrapleural pressure was -4 , -8 , and the left intrapleural pressure -8 , 0 . Ten cubic centimeters of air injected into the balloon, which had been placed in the posterior mediastinum, caused a slight drop in blood pressure; after an additional 10 cc. of air had been injected, there was a gradual rise in blood pressure. The blood pressure remained unaffected after another 20 cc. of air had been injected. The roentgenograms showed no evidence of pneumothorax. The left intrapleural pressure was -6 , 0 , and the right intrapleural pressure -6 , 0 . Some of the air had in the meanwhile undoubtedly regurgitated. It was only after another 20 cc. of air and 6 cc. of iodized oil had been introduced into the rubber balloon that the left intrapleural pressure became -4 , $+2$, and the right intrapleural pressure -2 , $+1$. The animal died shortly afterward.

Postmortem examination showed the posterior mediastinum to be distended. There was a slight rent in the rubber balloon and some iodized oil had escaped. The anterior mediastinal septum and the heart were pushed over to the left. It is thus to be noted that in spite of an undoubted slight right-sided pneumothorax the mediastinal contents were apparently displaced to the same side as the pneumothorax. The diaphragm was not raised. The intercostal spaces were equal.

EXPERIMENT 3.—The same technic was employed that was used in experiments 1 and 2. After 5 cc. of air had been injected into the balloon, which had been placed in the posterior mediastinum, marked irregularity in the blood pressure and respiratory curve were noted. As the air in this experiment was injected by a syringe, it could be entirely released or kept in the balloon at will. A control



Fig. 1.—In *A*, note the rubber balloon which has been placed into the posterior mediastinum and inflated by 25 cc. of air. The balloon has also been visualized by making injections of iodized oil into it. The heart has been compressed against the sternum. During the experiment the balloon burst and air escaped into the posterior mediastinum, where it can be seen. *B* shows the same as *A*, except that 2.5 cc. of iodized oil has been injected intratracheally.

roentgenogram taken at this period showed no evidence of pneumothorax. The left intrapleural pressure was $-4, 0$, and the right intrapleural pressure $-2, 0$. Five cubic centimeters of iodized oil was then injected into the rubber balloon so that it could be visualized. This act was followed by extreme irregularities in the blood pressure curve, as the record indicates. The respiratory curve showed but slight oscillation. The trachea was undoubtedly compressed, and the resulting forced respiratory efforts were responsible for the marked changes in blood pressure. Several plates were then taken, and the lateral view (fig. 1 *A*) suggested that some air had escaped into the mediastinum and perhaps into the pleural cavities. It was impossible to obtain any definite readings with the

pneumothorax needle because of the tracheal compression and consequent lack of respiratory excursion. The animal died in asphyxia, and a roentgenogram taken immediately after death showed the heart to be markedly dilated. The amount of cardiac dilatation was more than could have been expected even if the heart had ceased beating during diastole. The lower end of the rubber balloon was found to extend well down over the heart, and it had undoubtedly hindered heart action. A small amount of iodized oil was found in the right side of the thorax. The vessels of both hila were full, engorged and constricted above the engorgement, particularly the vessels of the right hilum. There was a small amount of clear fluid and air in the pericardial sac. The balloon was still much distended and also occupied the greater part of the posterior mediastinum. A small rent in the balloon was discovered. The left lung was fully distended, that is, in almost full inspiration. The right lung was somewhat shrunken and atelectatic, but not in

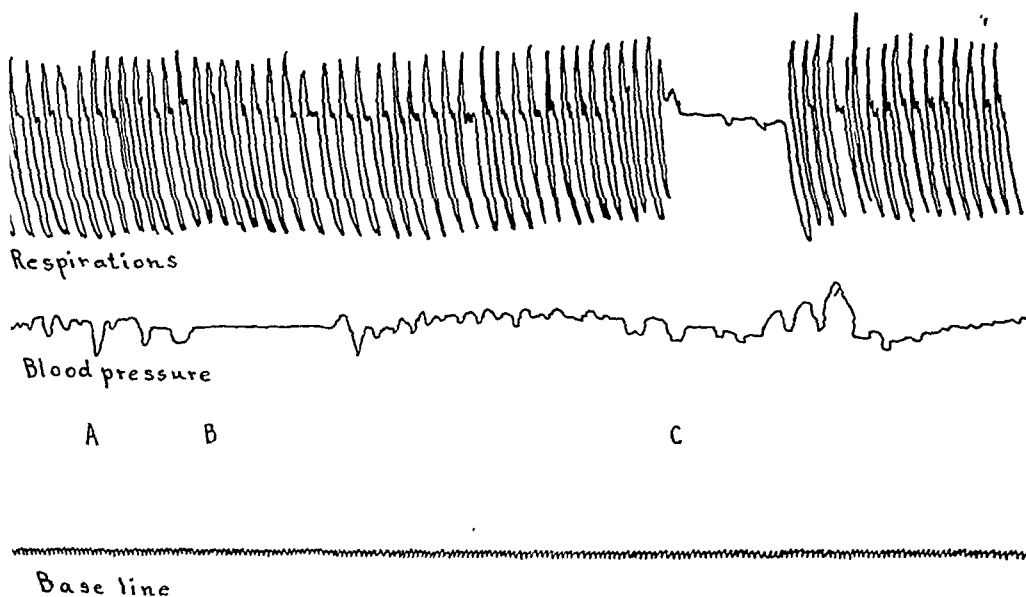


Fig. 2 (experiment S).—On Dec. 5, 1928, a rabbit weighing 3 Kg. was given 1.1 Gm. of sodium barbital intraperitoneally. A rubber balloon was placed in the posterior mediastinum and was connected with a syringe. Six cubic centimeters of air had previously been injected but allowed to escape. At A, 2 cc. of air was injected and then allowed to escape from the balloon. At B, 5 cc of air was injected, and the blood pressure curve was registered as a straight line. When the injected air was allowed to escape, the blood pressure was again registered. At C, 4 cc. more air was injected and temporarily not allowed to escape from a rubber balloon which this time compressed the trachea.

the phase of what would be considered complete and full expiration. The right lung showed marked patchy pulmonary emphysema. The upper lobe of the left lung showed peripheral emphysema. Both lungs were congested, particularly the right. The inferior vena cava was compressed at one point. This was perhaps due to the downward displacement of both diaphragms and also to the presence of free air in the posterior mediastinum. The posterior mediastinum was so distended that on ordinary inspection of the roentgenogram just after death a pneumothorax was suspected.

The initial change in the blood pressure following the injection of air into the rubber balloon which was placed in the mediastinum was always a fall in blood pressure. This fall in blood pressure was perhaps more marked when the balloon was in the anterior mediastinum. This might be expected, for a sudden increase in the vertical diameter of the rubber balloon would of necessity more directly impair heart action and be more likely to compress the great vessels. Compression of blood vessels, particularly of veins, was found constantly in this series of experiments. If when the blood vessels at the root of the lung were compressed the main bronchus was also encroached on, then the lung would be even more collapsed (hypoventilation) although peripheral emphysema could be present and the corresponding diaphragm not necessarily elevated. The opposite lung would be overdistended and give evidence of marked compensatory emphysema (hyperventilation). The liver was also observed to be engorged on several occasions. We did not observe any such gross changes in the spleen, but such changes were suggested in the kidneys on three occasions.

When the foregoing experiments were repeated and the injected air aspirated or allowed to escape, then the blood pressure and respirations which were registered as a straight line would immediately return to normal. Throughout such an experiment it would be the blood pressure and not the respirations which would show the most marked changes. If the mediastinum is repeatedly acutely distended and the trachea or a main bronchus compressed, then pulmonary emphysema will usually develop.

Graham⁸ has shown that distention of the capillaries induces a diminution rather than an increase in the size of the alveoli. He was able to show experimentally that the alveoli of the lobe the capillaries of which were distended were much smaller than the alveoli the capillaries of which were not distended.

TRACHEAL FISTULAS

By cutting out windows in the trachea at various levels, it was possible to study the production of mediastinal and subcutaneous emphysema in a manner which is quite similar to that occurring in man as a result of injuries to the trachea and bronchi.

When the trachea was being operated on, slight irregularities in the blood pressure and respiratory curves were noted but there was soon a return to normal. When a window was made in the trachea low down and posteriorly, then mediastinal emphysema developed fairly regularly. The emphysema extended to the anterior mediastinum and was to be

8. Graham, E. A.: Cautery Pneumectomy, personal communication to the authors.

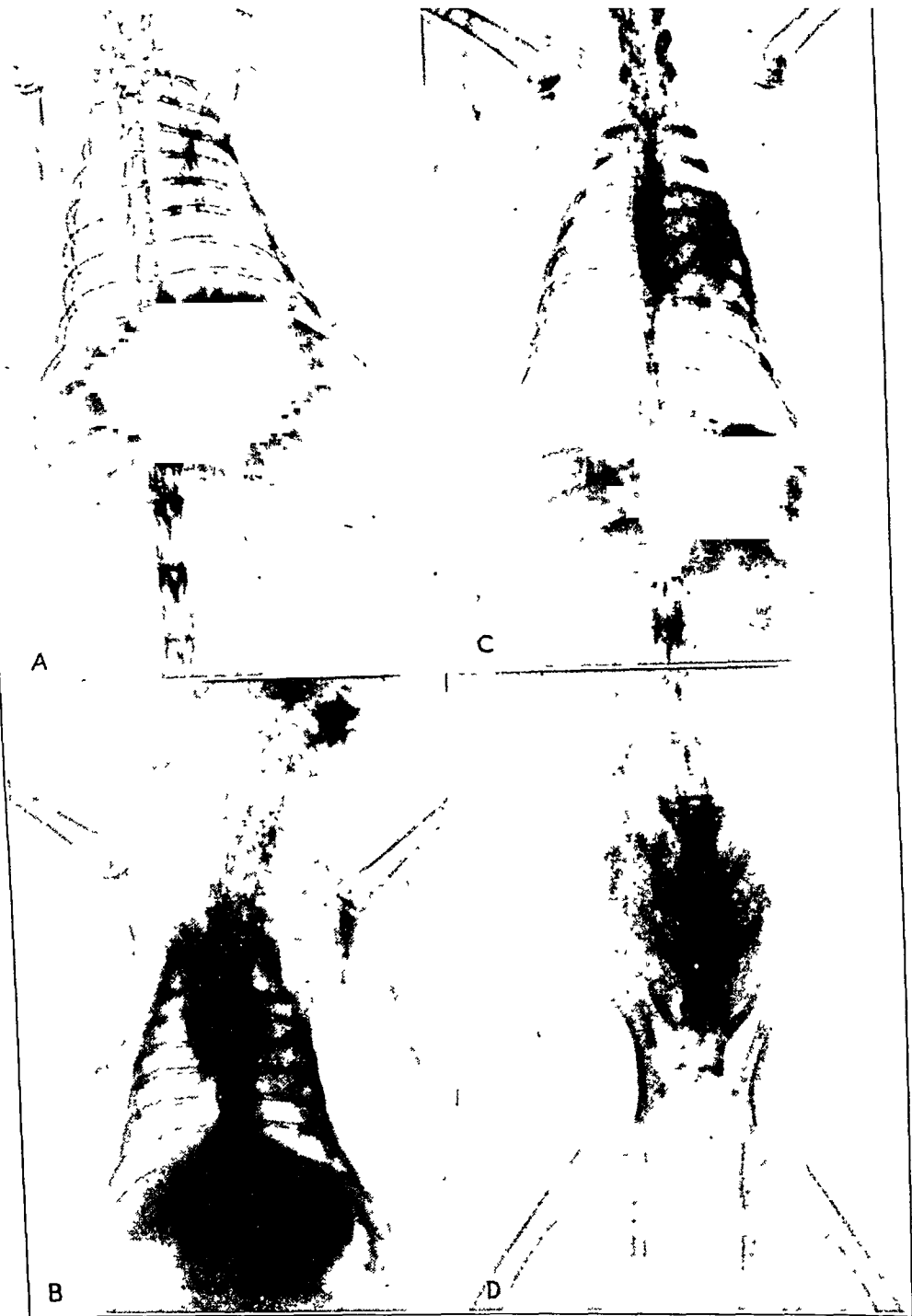


Fig. 3 (experiment 4) — *A*, normal control plate. *C* shows that the thorax has increased in size. The diaphragm has descended. The intercostal spaces are widened. The heart has been displaced to the right. Air has dissected retroperitoneally and has outlined the kidneys and perirenal tissues and has even extended to the lower limbs. In *B*, note the tremendous subcutaneous emphysema which developed in a rabbit consequent to the production of an experimental tracheal fistula. Note also the sharp outline of the muscles of the neck and of the skeleton, and the size and position of the heart, diaphragm and the thorax as a whole. Plates of the upper (*C*) and lower (*D*) portions of the body have been joined to each other to give a view of the whole body.

particularly noted dissecting up the mediastinal surface of the sternum. It also spread to the limbs over the anterior wall of the chest and in the axillae following along the fascial sheaths of the axillary vessels. The thorax on certain occasions actually increased in size, as the following experiment demonstrates.

EXPERIMENT 4.—At 10:40 a. m., control roentgenograms were taken. A triangular window was then made in the trachea posteriorly and low down. The trachea was then allowed to drop back and the muscles and skin sutured tightly. A lateral roentgenogram showed that the thorax had definitely increased in size. At 11:05 a. m., the left intrapleural pressure was -6 , -4 and the right intrapleural pressure -2 , -7 . At 2 p. m. (fig. 3, *B* and *D*), marked subcutaneous emphysema was noted. Marked collections of air were to be noted in the neck and axillae and to a lesser degree along the lateral aspects of the lower abdominal wall. Posteriorly, the emphysema stopped at the superior nuchal line. At 2:05 p. m., both intrapleural pressures were -6 , 0 . The animal had been under great respiratory distress for some time. Dyspnea was marked and respirations were noisy. The animal was then photographed. After a few convulsive kicks, the animal died (4:25 p. m.). Roentgenograms were now taken and showed that the thoracic cavity had increased in size. The intercostal spaces were widened and the heart definitely displaced to the right. The extensive emphysema presented a picture which suggested a bilateral pneumothorax.

Both kidneys appeared to be outlined by air which had dissected down into the retroperitoneal spaces. That such was the case was verified at necropsy. The x-ray shadow which suggested an air outline of the kidneys and perirenal tissue could be definitely differentiated from the diaphragm. Emphysema of a considerable degree could be observed in the anterior and posterior mediastina. Both lungs showed evidences of pulmonary emphysema.

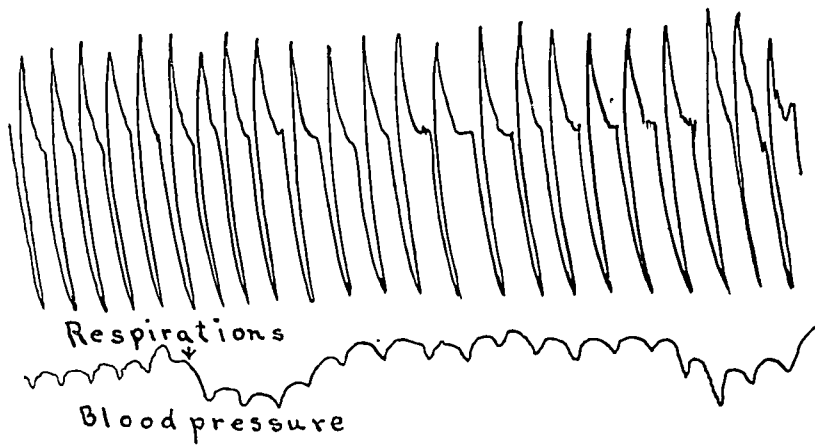
THE COURSE AIR MAY TAKE IN THE PRODUCTION OF MEDIASTINAL AND SUBCUTANEOUS EMPHYSEMA

The air which reaches the mediastinum may take several courses. It may spread subfascially (Brauer⁹), that is, between the costal pleura and the intrathoracic fascia. In man, air which collects in the mediastinum may give a sharp contour to the great vessels.

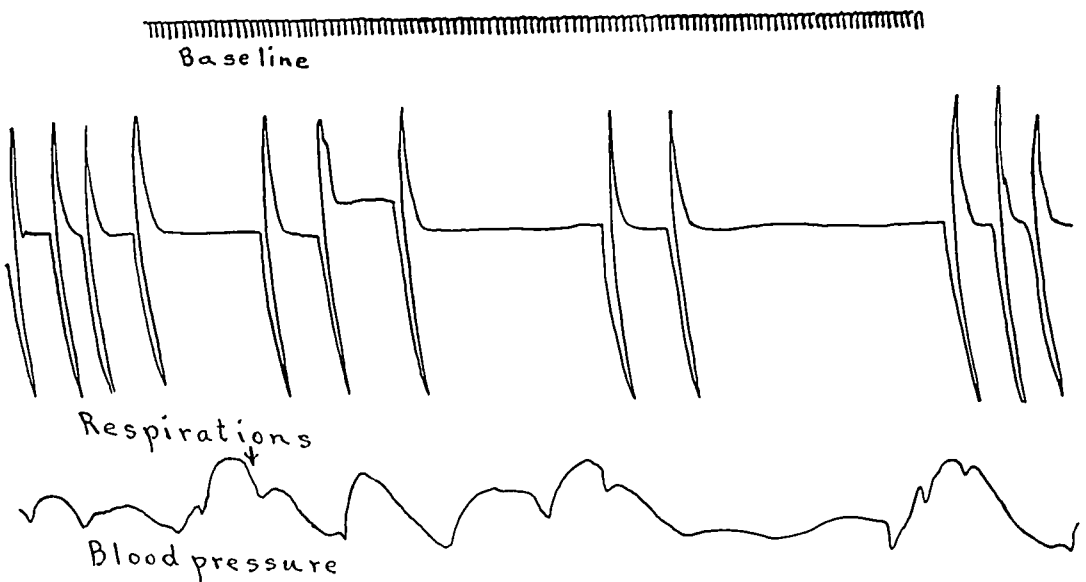
The most severe type of mediastinal emphysema results, as Sercer and Peicic¹⁰ have pointed out, when the lung itself is injured, as during pneumothorax treatment. So, too, rupture of an emphysematous bleb or of a cavity may allow air to dissect at first interstitially and then to the hilum of the lung; from thence into the mediastinum subfascially and even over the entire body. It is possible for air to dissect up all along the trachea to the floor of the mouth, extending under the base of the tongue which becomes raised. So, too, it is well to remember that the air follows with predilection the normal fascial planes, particularly the sheaths which surround blood vessels. The axillary and femoral

9. Brauer, cited by Sercer and Peicic: *Beitr. z. Klin. d. Tuberk.* **53**:123, 1922.

10. Sercer, A., and Peicic, R.: *Ein Beitrag zur Kasuistik der Todesfälle beim künstlichen Pneumothorax*, *Beitr. z. Klin. d. Tuberk.* **53**:123, 1922.



A



B

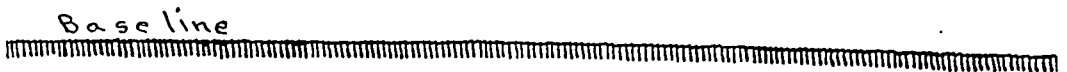


Fig. 4.—In *A*, the two drops in blood pressure noted in the curve represent the effect of the injection of 10 cc. of air into the anterior mediastinum. *B*, this portion of the original tracing (*A*) was recorded after 10 cc. of air had been injected into the anterior mediastinum. This amount was injected over a period of about one hour in five separate amounts.

vessels may thus be compressed. Then again, not only may the air extend retroperitoneally and outline the kidneys, but we have observed it around the renal vessels and ureter.

When the trachea is injured then the air may dissect downward, and when it dissects from above down, the subcutaneous emphysema is usually marked and mediastinal emphysema exists to a lesser degree. Severe mediastinal emphysema may also develop from a tension pneumothorax.



Fig. 5.—Anterior mediastinal emphysema. A window has been made in the lateral wall of the chest and the lungs have been allowed to drop back. Air had previously been injected into the anterior mediastinum. Note the emphysematous blebs in the loose tissue of the anterior mediastinum. The pericardium, which also shows emphysematous blebs, has been opened.

EXPERIMENT 5.—At 3:47 p. m., the initial right intrapleural pressure was —6, —8, and the left —8, —10. A low left anterior tracheotomy was performed. At 4:20 p. m., the blood pressure registered 95 mm. of mercury, which indicated a slight rise. At this stage of the experiment pressure on the animal's neck or axillae would cause a slight drop in blood pressure. At 4:34 p. m., the blood pressure was 100 and both pleural pressures —12, —10. The animal's limbs were

then released. This relieved skin tension. Slightly more subcutaneous emphysema then developed. At 5:08 p. m., the left intrapleural pressure was -2 , -10 , and the right intrapleural pressure -8 , -6 . The skin over the neck was bluish. The blood pressure was 45 mm. of mercury. Respirations were now labored and rapid. Definite emphysema could be observed over the right side of the thorax. The entire thorax seemed to move as a whole. At times the excursions of the right side of the chest were a little more marked than the left. The fistula in this animal was so placed that the surrounding tissue could partially occlude it; hence, mediastinal emphysema was not marked. In none of these experiments did the

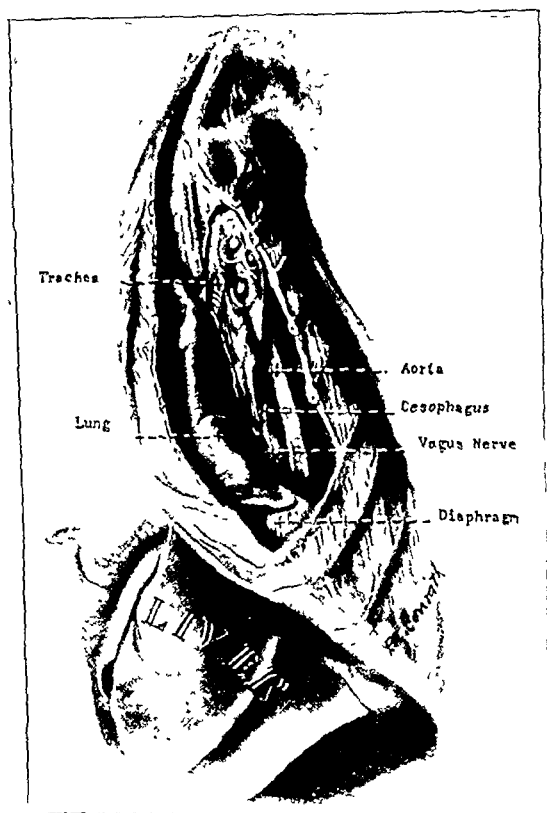


Fig. 6.—Posterior mediastinal emphysema. Drawing from actual specimen. Note how the "emphysema" surrounds and compresses the trachea, esophagus and vessels at the root of the lung. The right lung is somewhat collapsed.

injected iodized oil make its way into the mediastinum. This was, in all probability, due to the accumulation of secretions within the trachea, to the viscosity of the oil and to the fact that the surrounding tissues always partially occluded the opening in the trachea.

In the foregoing experiments with tracheal fistulas, when mediastinal emphysema was marked, then subcutaneous emphysema was slight, and vice versa. The animals in these experiments usually died from the

consequences of mediastinal and subcutaneous emphysema, from mediastinitis, or from a pneumonic process which was usually severe. Combinations of the foregoing conditions also occurred. Thus, in animal 4, a window had been made in the trachea low down and posteriorly. The animal died on the third day. Subcutaneous emphysema could be noted over the neck and thorax, and slight emphysema in the anterior and posterior mediastina. A pneumonic process could be demonstrated in the left upper lobe, also patches of pneumonia throughout the right lung. A whitish sticky secretion could be expressed from the trachea. The neck wound was quite clean, and the fistulous opening slightly infected.

Gold¹¹ has shown that in dislocating the thyroid gland during thyroidectomy air can be sucked into the mediastinum. He added that mediastinal emphysema is a typical complication of substernal strumectomy and that the collections of air which can be demonstrated remain for some time. He further noted that the treatment of mediastinal emphysema with the negative pressure apparatus ("Unterdruck Apparat Lebsche-Sauerbruch") does not give satisfactory results in such cases. It is not uncommon to find blood staining the entire mediastinum after operations in the neck.

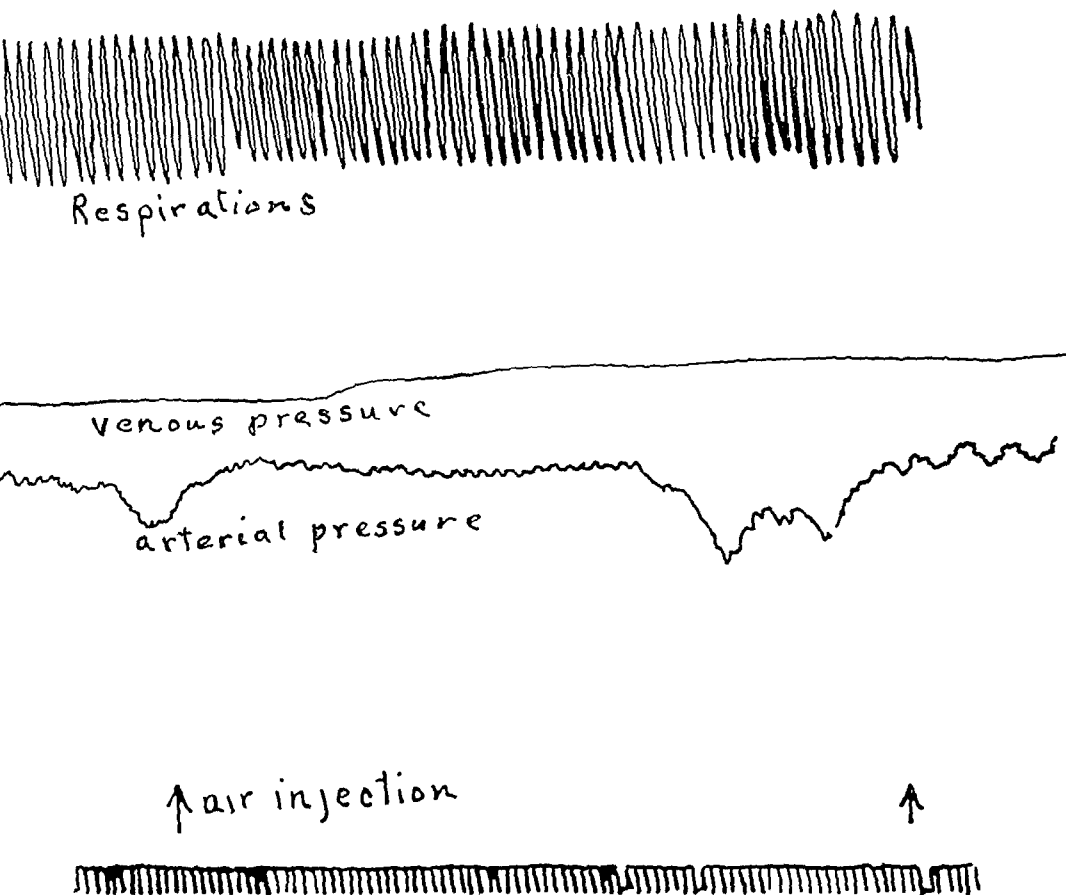
Mediastinal emphysema has been observed after pulmonary lobectomy, both clinically and experimentally. Graham,⁸ in a large series of cautery pneumectomies, never observed mediastinal emphysema after this procedure. In a series of experiments on lung healing (Olch and Ballon¹²), although portions of lung tissue were excised and middle sized bronchi were cut across, in no instance did mediastinal emphysema develop. In one animal, at the suggestion of Dr. Graham, large bronchi were cut across and were then intentionally sutured so that there was absolutely no apposition of the cut ends of the bronchi. Tremendous mediastinal and subcutaneous emphysema resulted. The animal died on the fourth day. The lung wound appeared to be healed. An injection of iodized oil failed to show any injection of the lung tissue beyond the points where the bronchi had been cut off. Although some air may have escaped into the pleural cavities, quantities of air must also have escaped from the interstitial tissue to the root of the lung. In this instance air was noted even under the base of the tongue and around the ureter.

11. Gold, E.: Ueber Mediastinal-emphysem nach Strumektomie, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **37**:352, 1924; discussion in Arch. f. klin. Chir. **138**:193. 1925.

12. Olch, I. Y., and Ballon, Harry C.: Experimental Lung Abscess Following Ligation of the Pulmonary Artery, unpublished communication.

THE EFFECTS OF THE INJECTION OF AIR INTO THE
ANTERIOR AND POSTERIOR MEDIASTINA

We noted in the following experiments that when the injected air was given sufficient time to spread and diffuse, the blood pressure would



③ 10cc

15cc

Fig. 7.—Tracing which shows the changes in venous pressure and arterial pressure following the injection of small quantities of air into the anterior mediastinum.

again return to normal in several instances. For, if the quantity of air injected were not too great, then after the air had diffused the heart action would become free. It has been shown, and we were able to verify the fact, that large amounts of blood can apparently become stag-

nant in the lung without producing marked pressure changes in either the greater or lesser circulations (Straub¹³).

It is also to be noted that mediastinal pressure can become definitely positive before pneumothorax need develop.

EXPERIMENT 6.—A rabbit weighing 2 Kg. was given 1 Gm. of sodium barbital intraperitoneally and was prepared in the usual way. The initial intrapleural and mediastinal pressures were all negative. After 150 cc. of air had been introduced into the mediastinum, the right and left pleural pressures were 0, —6. The mediastinal pressure was +2. Two roentgenograms were then taken but did not show any evidence of pneumothorax. Shortly afterward, the left intrapleural pressure became +6, the right —10, —5 and mediastinal pressure 0. Further



Fig. 8.—Right pneumothorax. This figure demonstrates that unilateral pneumothorax is possible in a rabbit. The bronchial tree has been outlined by the injection of iodized oil. An ordinary roentgenogram in this instance suggested a bilateral pneumothorax.

injection of air produced asphyxia and caused the death of the animal. The left side of the diaphragm was found to be ballooned out, almost eventrated and much lower than the right side. The heart was compressed against the sternum and the left lung slightly collapsed. There were evidences of anterior and posterior mediastinal emphysema.

EXPERIMENT 7.—A rabbit, weighing 2.6 Kg., received 0.78 Gm. of sodium barbital intraperitoneally, and adequate general anesthesia was given. Air was then injected into the anterior mediastinum through a needle which was connected

13. Straub, H.: Ueber den kleinen Kreislauf, *Deutsches Arch. f. klin. Med.* 121:394, 1917.

with a pneumothorax apparatus. The right intrapleural pressure was 0, the left intrapleural pressure -4 , -2 , and mediastinal pressure -2 , -4 . After control plates had been taken, 75 cc. of air was injected into the anterior mediastinum. The right intrapleural pressure was then -4 , -6 , and the left -4 , -7 . Another 50 cc. of air was then injected. A fall in blood pressure, an increase in the respiratory rate and a shortening of the respiratory excursion followed. The blood pressure soon returned to normal, although the respirations continued to be shallow. Another 50 cc of air was injected and produced even a more marked drop in blood pressure. The left intrapleural pressure was $+2$, $+6$, and the right

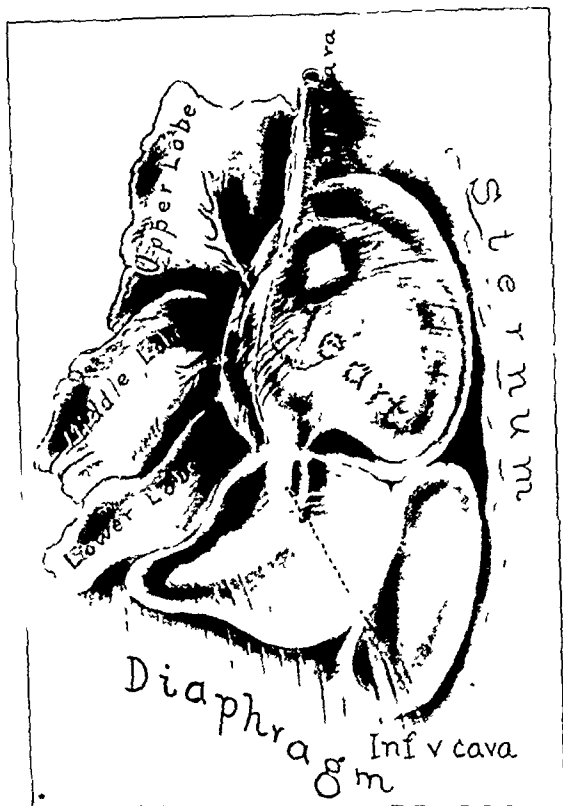


Fig. 9.—Heart tamponade. This drawing illustrates an experimentally produced hemopneumopericardium. The heart muscle had been directly lacerated. Air entered the pericardium and also the anterior and posterior mediastina and produced the large emphysematous blebs which compressed the lungs, as illustrated. These emphysematous blebs occupied the greater portion of the lower part of the thorax and suggested the presence of a pneumothorax.

-4 , -6 . From this stage on, whenever the pneumothorax needle was introduced into the pleural cavity a definite but temporary fall in blood pressure would occur. After another 50 cc. of air had been injected, the mediastinal pressure became $+8$, the left intrapleural pressure $+6$, $+8$, and the right $+2$. A marked fall in blood pressure was now observed. Respirations were regular. Five minutes after this last injection of air, the animal began to show definite signs of asphyxia. The

left intrapleural pressure was then +22, and the right +6 (cm. of water). The roentgenogram revealed a definite left-sided pneumothorax and suggested the presence of a small amount of air in the right costophrenic angle. The animal soon died. The heart and mediastinal contents were found to be displaced well over to the left. Subcutaneous emphysema and mediastinal emphysema were evident. No mediastinal tear could be demonstrated even though iodized oil was injected into the mediastinum under considerable pressure. The pressure exerted, however, may have been entirely expended in forcing the iodized oil through the needle.

It becomes evident that just as mediastinal emphysema may be a consequence of a pneumothorax, so may a pneumothorax in certain instances undoubtedly be due to what was originally a mediastinal emphysema. Sauerbruch¹⁴ has shown that mediastinal emphysema may be a consequence of a tension pneumothorax and that the reverse may also occur. It would, therefore, seem likely that a tension pneumothorax may later develop into a mediastinal emphysema, the result of a pneumothorax or even of mediastinal emphysema. It is well to remember that the cardinal signs of penetrating wounds of the thorax are subcutaneous emphysema, pneumothorax and bleeding (Haim¹⁵). If the lung itself has been injured, then the subcutaneous emphysema is usually an expression of mediastinal emphysema. In a discussion on injuries of the lungs as a result of contusions of the wall of the chest, Sauerbruch¹⁶ noted that, if the trachea is tied off and the wall of the chest traumatized, in 50 per cent of instances in the experimental animal a rupture of the lung will occur. One of the consequences is pneumothorax, and it is in such cases as we have already noted that the severest type of mediastinal emphysema may develop. Before mediastinal emphysema does develop, however, the affected pleural cavity becomes distended and the lung collapsed. The enclosed air, therefore, can compress the heart, other mediastinal contents and the opposite lung. Air continues to enter the affected thorax even though the lung is collapsed because air can enter the main bronchus and can escape through the tear in the lung. If there is in addition a tear in the mediastinal pleura, then a tension pneumothorax may develop and subsequently mediastinal and subcutaneous emphysema.

It has been shown that the lung tissue may be so injured that when air enters through the bronchus it can escape into the loose tissues, but that during expiration the injured lung tissue around the open bronchus

14 Sauerbruch, F. Die Bedeutung des Mediastinal-emphysems in der Pathologie des Spannungs-pneumothorax, Beitr. z. klin. Chir. **60**:450, 1908.

15 Haim. Ueber penetrierende Thoraxverletzungen, Deutsche Ztschr. f. Chir. **79**:269, 1905.

16 Sauerbruch, F. Die Chirurgie der Brustorgane, Berlin, Julius Springer, 1925.

is sucked into the lumen of the tear in the lung if it includes a bronchus; hence, the inspired air which has been drawn into the injured pleural cavity cannot be expired and cannot escape except through the routes previously mentioned. Pain could also cause a splinting of the affected side; and as cough when the glottis is closed would tend to increase the intrapulmonary pressure, this factor would also tend to keep the tear in the lung from closing.

It is difficult to prove that the mediastinum which separates the pleural cavities enables them to function independently. Figure 8 shows how in a unilateral pneumothorax in a rabbit the mediastinal contents can be pushed right over into the opposite side of the chest. This observation, of course, agrees fully with the mobility of the human mediastinum and the tendency of changed pressures to become equalized throughout the thorax, which were extensively discussed by Graham. We studied the degree of pneumothorax which developed after death in one animal. We observed no evidence of pneumothorax fifty-five minutes after the death of the animal.

In determining venous pressures by the method already referred to, no sharp sudden changes were noted. Only gradual rises and falls in the venous pressure were observed. By the method which we employed, it is occasionally possible to demonstrate slight changes with the phases of respiration. In animal 14, air in quantities of 10 cc. was injected into the anterior mediastinum and rises of 3 cc. were noted in the water manometer. Our experiences with venous pressures in these experiments do not permit us to make any absolute statements. For at times the injection of a small quantity into the mediastinum will produce a rise in venous pressures and on other occasions a drop. Nor need there be, according to our present experience, a rise in venous pressure when there is a fall in arterial pressure, although transitory terminal rises in venous pressure (preasphyxial and asphyxial) concomitant with the fall in arterial pressure could be observed.

The following experiment illustrates how the picture of pressure on the pericardium and of heart tamponade resembles that due to mediastinal emphysema (Sauerbruch).

HEART TAMPONADE

The left intrapleural pressure was -4 , -12 , and the right intrapleural pressure -6 , -10 . Whenever a needle was pressed against the pericardium, slight irregular falls in blood pressure were noted. The blood pressure quickly recovered when the needle was withdrawn. When the needle was inserted into the pericardium from the lower end of the sternum, then a drop in blood pressure of 20 mm. of mercury was noted. Any pressure on the needle, no matter where it was placed over the heart, always caused a fall in blood pressure. The fall in blood pressure was apparently directly proportional to the pressure exerted. No significant changes in respiration were noted, although the respiratory excursion

sometimes became smaller and the rate somewhat slowed. When an incision was made over the lower aspect of the sternum, then the blood pressure dropped and grew irregular, and respirations became rapid. When a large sucking wound had been produced in the pericardium, the animal soon succumbed. At necropsy, a small opening was found in the pericardium. A hemopneumopericardium was present. There were also large emphysematous blebs in the anterior mediastinum and some emphysema in the posterior mediastinum. The lungs showed marked peripheral emphysema.

It is to be noted that some blood escaped from the animal's mouth before death. Where this blood came from was not quite certain. It is known that when the intrapulmonary pressure is reduced, bleeding from the lung may occur



Fig. 10.—Introduction of a solid into the anterior mediastinum. Three cubic centimeters of a mixture of paraffin and iodized oil have been injected into the anterior mediastinum and have solidified. This mass caused some compression of the mediastinal contents, particularly of the trachea. The animal died of edema of the lungs. There were, in addition, some evidences of pulmonary emphysema. The heart was large. The tracheal mucous membrane was reddened.

(Hoffmann¹⁷). The question might be raised, however, as to whether or not the pulmonary emphysema in this case may not have been due to some aspirated blood. The roentgenograms taken after death were misleading because the emphysematous blebs crowded the left side of the thorax and therefore suggested a pneumothorax. The liver was somewhat engorged with blood. The more immediate cause of the death of the animal was undoubtedly due to the effects of the so-called heart tamponade.

17. Hoffmann, F. A. *Erkrankungen des Mediastinums*, in Nothnagel: *Specielle Pathologie und Therapie*, 1896, vol. 13, p. 1.

EFFECTS OF THE INJECTION OF MIXTURES OF PARAFFIN AND
IODIZED OIL INTO THE ANTERIOR AND
POSTERIOR MEDIASTINA

The effects of the injection of paraffin and iodized oil into the mediastinum depends entirely on the size and position which the mixture occupies after it has solidified. All substances that we used failed to produce any immediate irritative reactions. It is well to remember, however, that if the trachea or esophagus is transfixcd, inflammatory processes may result (Ballon¹⁸).



Fig. 11.—Intrathoracic hernia *A* indicates air in the posterior mediastinum; *B*, the stomach with a small amount of iodized oil in it, *C*, how the lungs are compressed against the vertebral column, and *D*, the irregularity of the diaphragm

When solids are placed above the jugulum, they may produce absolutely no distress. They can, however, compress blood vessels, particularly veins and, although the pressure within these compressed veins may undoubtedly increase, still nothing more than that these veins become dilated need occur, although local parts through pressure might thus be somewhat deprived of their nutrition. One rabbit which received a substernal injection of a mixture of 3 cc. of iodized oil and paraffin showed no immediate distress but during the day died of what proved to be edema of the lungs. In another instance, the injection of

18. Ballon, H. C.: Lipiodol bei der Lungentuberkulose; Eine experimentelle klinische und pathologische Studie, Frankfurt. Ztschr. f. Path. **36**:207, 1928.

a similar amount of the same mixture failed to produce any change in the blood pressure or in the respirations. When a slight pressure which under ordinary circumstances would have produced no effect was then applied to the thorax, irregularities in the amplitude of the respiratory excursions were noted which disappeared when the pressure was removed. The same occurred when pressure was exerted over the thorax after some of the injected mass had been allowed to solidify over the heart.

If a needle which had been introduced into the mediastinum was merely allowed to rest on the great vessels, a slight fall in arterial blood pressure and irregularities in the respiratory curve were noted. If air in quantities of a few cubic centimeters was then injected, further slight falls in arterial blood pressure were noted and the respiratory excursions became smaller.

It would seem that a fluid can spread almost as readily along the anterior mediastinum as along the posterior mediastinum. A solid mass in the anterior mediastinum of sufficient size to compress the lung must of necessity at the same time compress some of the blood vessels. At necropsy all that may be noted when such is the case is slight lateral compression of the trachea, edema of the tracheobronchial mucous membrane and some pulmonary emphysema.

It is interesting to note that Gaisford¹⁹ passed an endotracheal catheter before death in six children who died from status thymico-lymphaticus. There was no evidence of tracheal compression, although the tracheal mucous membrane was slightly injected. The introduction of air through the catheter failed to improve the cyanosis or dyspnea. At post mortem, the large vessels of the neck were found dilated.

Nissen²⁰ has shown that when substances, practically the same as those which we employed, were injected into the mediastina of rabbits and allowed to remain there over a considerable period of time the changes in blood pressure noted were similar to those which we have already described.

Nissen and Cokkalis²¹ have shown that prolonged tracheal stenosis leads to hypertrophy and dilatation of the right side of the heart. The edema of the lungs which may develop in this connection predisposes to bronchopneumonia. They apparently consider that the edema of the lungs which develops in tracheal stenosis is due to (1) the sudden

19. Gaisford, W.: Status Thymico-Lymphaticus, personal communication to the authors.

20. Nissen, R.: Experimentelle Untersuchungen zur Theorie des Entstehung des Lungenemphysems, Deutsche Ztschr. f. Chir. **200**:177, 1927.

21. Nissen, R., and Cokkalis, P.: Experimentelle Untersuchungen ueber mechanische Atmungsstörungen und einige Folgezustand, Deutsche Ztschr. f. Chir. **194**:50, 1925.

reduction in intra-alveolar pressure within the emphysematous nonyielding alveoli and (2) the impaired action of the hypertrophied right ventricle (Cohnheim-Welch). The amount of blood in the lung will therefore depend not only on the size of the lung but also on the state of the entire thorax, including the position of the diaphragm.

Changes in either intrapleural or mediastinal pressure must affect the intra-alveolar pressure in some way or other.

The pulmonary emphysema which may develop consequent to mediastinal emphysema also tends to narrow the mediastinum. Widening of the thorax in the experimental animal (Nissen²²) does not lead to hyperventilation or to substantial emphysema. Widening of the thorax occurs only when the acting mechanism which will produce pulmonary emphysema lies directly or indirectly in relation to the tracheobronchial tree (Alexander and Kountz²³). Hyperventilation and emphysema are but degrees of the same process, according to Aschoff and Tendeloo. Hypoventilation and atelectasis may therefore be considered phases of the reverse condition.

In no instance did we observe grossly any evidence of edema of the mediastinum, and fluid in the pleural cavity in only one instance. This occurred when mediastinal emphysema developed from the subcutaneous injection of air.

Concerning the absence of mediastinal edema in any of our animals which developed mediastinal emphysema, it will perhaps not be amiss to refer to a recent paper by Granström.²⁴ He remarked that he often found signs of dulness to the right of the sternum which apparently developed from and had something to do with stasis in the larger vessels of the thorax. He mentioned that the lesion of the heart in such instances was either one of myocarditis, aortic or mitral endocarditis, or arteriosclerosis. Pulmonary emphysema was present in some but absent in others. The heart was sometimes small and, at other times, enlarged. Granström also observed the condition which he considers to be mediastinal edema in patients suffering from heart disease who showed no evidence of "Stauungserscheinungen" elsewhere. He noted further that the extensive edema in the anterior mediastinum may displace the medial lung border of the upper lobes outward and that portions of the lobes so displaced may become airless. Some of Granström's patients have come

22. Nissen, R.: Kreislaufwirkung umschriebener Drucksteigerung im Mittelfellraum, *Deutsche Ztschr. f. Chir.* **208**:59, 1928.

23. Alexander, R. L., and Kountz, W. E.: *Studies on Emphysema*, to be published.

24. Granström, E.: Ueber Erweiterung der vena cava superior und anonymae und ueber Oedem des Mediastinums bei Herzinsuffizienz, *Wien. klin. Wchnschr.* **9**:264 (Feb. 28) 1929.

to necropsy. Granström also noted that in certain severe cases of pulmonary emphysema this mediastinal edema may be absent, and that it may be present when there is no pulmonary emphysema. Widening of the superior vena cava and the innominate veins is in his estimation directly responsible for the mediastinal edema.

It is to be remembered that the great vessels may become elongated and tortuous in certain cardiac conditions and yet the size of the heart remains unaffected. In this way any elongation of the aorta makes the subclavian arteries more readily palpable.

The following experiment concerns an artificially produced intrathoracic hernia which for the most part occupied the inferior portion of the posterior mediastinum. This condition must be differentiated from mediastinal hernia which is really a gaseous displacement of the mediastinum but which may in turn be aggravated by any increase in intramediastinal pressure.

MEDIASTINAL INTRATHORACIC HERNIA

RABBIT 7.—To an animal weighing 2.9 Kg., 8.7 cc. of sodium barbital was given intraperitoneally. Right intrapleural pressure was -4 , -6 , and left intrapleural pressure -4 . An incision was made in the midline. A slight fall in blood pressure was noted when the peritoneal cavity was opened and the abdominal organs, particularly the stomach, were handled. If they were left alone then the blood pressure would rise beyond its former height. Respirations would be slightly irregular and expiration at times quite deep. When the left side of the diaphragm was pushed up from below, then the respiratory and blood pressure excursions became less marked. The esophageal portion of the stomach was then mobilized. This act caused a marked temporary drop in blood pressure. Any pull on the stomach or gastrohepatic ligament produced irregularities in the blood pressure and respirations. This was particularly marked when that portion of the stomach which received the main vagus fibers was handled. A general increase in blood pressure resulted from the latter procedure. The mobilized part of the cardiac portion of the esophagus and a small portion of the esophagus could now be herniated through the esophageal opening of the diaphragm. Respirations now became irregular, and the blood pressure began to fall. The intra-abdominal portion of the stomach became dilated. Both diaphragms were elevated. The animal died soon after the abdomen was closed. Injections of iodized oil were made into the esophagus and lungs. Necropsy verified the roentgen observations. There was slight mediastinal emphysema, air having entered the thorax through the esophageal opening of the diaphragm. Both lungs were compressed. The heart was pushed up against the sternum, the inferior vena cava against the vertebral column.

Just as an increase in the size of the mediastinal contents may affect the position of the diaphragm, so may the position of the diaphragm affect the position of the structures in the mediastinum, particularly when there are pleuropericardial adhesions. Any process which encroaches on the costophrenic angle or the mediastinum may narrow

the space occupied by the inferior vena cava and appreciably disturb the inflow of blood through the inferior vena cava. An intrathoracic hernia through one of the normal openings in the diaphragm might readily accomplish this. When the margins of the lungs are pushed apart by anything which comes to occupy the anterior mediastinum, then the blood vessels in this neighborhood come to lie more directly on the vertebral column.

CAUSES OF SPONTANEOUS MEDIASTINAL EMPHYSEMA AS
REPORTED IN THE LITERATURE

Jehn and Nissen¹ have stated that mediastinal emphysema was once reported after a pneumoperitoneum.

We have also produced mediastinal emphysema by injecting air subcutaneously or directly into the lung. At the close of an experiment on changes in bronchial caliber (Francis²⁵) performed on a cat by forcing bismuth subcarbonate into the bronchial tree and stimulating the vagus nerve, large bubbles of air were observed in the posterior mediastinum. They had apparently resulted from the rupture of an emphysematous bleb.

Galliard²⁶ considered that interlobular, mediastinal and subcutaneous emphysema may follow senile pulmonary atrophy, tuberculous pneumonia and bronchopneumonia which complicate infectious diseases. The author also added that mediastinal emphysema may follow violent efforts during parturition and severe dyspnea due to cholera and reported such a case. The question can be raised as to whether the immediate dyspnea in some cases is not one of the causes rather than an effect of mediastinal emphysema.

The commonest cause of subcutaneous and mediastinal emphysema in children is the rupture of an alveolus and may occur in pneumonia, croup and pertussis. A case of mediastinal emphysema which developed in a child of 18 months during a fit of coughing, three days after the crisis of pneumonia, has been reported by Boehme.²⁷ The emphysema disappeared in four days and was attributed to a ruptured bronchus (?). Gehrt²⁸ reported four cases of subcutaneous emphysema in grip pneumonia associated with tracheal stenosis due to edema of the trachea.

25. Francis, B. F.: Changes in the Size and Shape of the Bronchi Following Vagus Stimulation, to be published.

26. Galliard, L.: L'emphysème du médiastin, Bull. et mém. Soc. méd. d. hôp. de Paris 10:199, 1893.

27. Boehme, Gustave F.: A Case of True Mediastinal Emphysema, M. Rec. 95:1052 (June 21) 1919.

28. Gehrt, J.: Hautemphysem und Stenose bei Grippe, Deutsche med. Wchnschr. 46:1052, 1920.

In two cases of pandemic influenza reported by Symmers²⁹ distended air vesicles near the apex of the lung had ruptured. The soft tissues in the supraclavicular spaces were crepitant with infiltrated air. In another instance the rupture had occurred near the root of the lung, and bullae could be demonstrated over the pericardium up the neck and extending down as far as the crests of the ilia. Chronic fibrinous bronchitis as a symptom of mediastinal compression has been suggested by Mulligan and Spencer.³⁰ They reported a case which concerned a boy, aged 7 years. The condition disappeared following roentgen treatment. The cause was thought to be pressure on the blood vessels of the lungs causing a "leakage" of fluid into the bronchial tree. Two patients who were operated on for carcinoma of the esophagus and who died of slow suffocation have been reported by Faure.³¹ A drain had been used in both instances. The author wrote, "I could plainly see that a large quantity of air penetrated the mediastinum at each inspiration." Perforation of the esophagus by spicules of bone may be followed by mediastinal and subcutaneous emphysema. Pearce³² published the report of a case which concerned a patient who apparently swallowed a spicule of bone. The patient died forty-eight hours after the onset of symptoms. Bilateral pneumothorax was present. Von Bokay³³ saw mediastinal emphysema develop only four times in 2,000 intubations in children. Baranger³⁴ reported a case of traumatic mediastinal emphysema. He treated the condition by making a transverse incision above the manubrium and by plunging his finger downward behind the sternum (Tiegel³⁵). This act was followed by a rush of gas. Because he thought that the condition was due to a valvular pneumothorax, he made an incision into the pleura and, finding a tension pneumothorax on the right side, relieved it and the patient recovered.

Mueller³⁶ has shown that the heart's action also helps to spread the air in the mediastinum and that the coarse bubbling noises which are to be heard over the precordium are expressions of collections of air which

29. Symmers, D.: Pathologic Similarity Between Pneumonia of Bubonic Plague and of Pandemic Influenza, *J. A. M. A.* **71**:1482 (Nov. 2) 1918.

30. Mulligan, P. B., and Spencer, R. D.: Chronic Fibrinous Bronchitis as a Symptom of Mediastinal Compression, *J. A. M. A.* **82**:791 (March 8) 1924.

31. Faure, F.: The Surgery of the Posterior Mediastinum: Its Past and Future, *Bull. Johns Hopkins Hosp.* **16**:125, 1905.

32. Pearce, W. H.: An Unusual Case of Emphysema, *Lancet* **2**:221, 1886.

33. Von Bokay, cited by Gehrt (footnote 28).

34. Baranger, M.: Un cas d'emphysème médiastinal traumatique, *Bull. et mém. Soc. nat. de chir.* **52**:1243, 1926.

35. Tiegel: Ein einfaches Verfahren zur Bekämpfung der Mediastinalenphysems, *Zentralbl. f. Chir.*, March 25, 1911, p. 420.

36. Mueller, cited by Gehrt (footnote 28).

are compressed between the heart and wall of the chest. Lenormant³⁷ was of the opinion that the chief danger in mediastinal emphysema is circulatory. He considered that the extreme dyspnea, the feebleness of heart action, the smallness, frequency and irregularity of the pulse, the cyanosis of the face, the distention of the neck and the coldness of the nose and extremities all verify this fact. Subcutaneous emphysema, he stated, is secondary. He cited one case which followed an injury. He opened the thorax and found the lungs riding on an enormously distended mediastinum. The vena azygos was the size of a thumb, and the inferior vena cava the size of a child's arm. He attempted to aspirate the air (Tiegel), and also made multiple incisions but all to no avail. "De la rupture pulmonaire chez les enfants et de l'emphysème général qui l'a succédé" was the title of a paper published by Ozanam³⁸ in 1854. The conclusions which he drew were as follows: All pulmonary conditions, all violent respiratory efforts, can cause a rupture of pulmonary tissue in the infant. Such a rupture is followed by internal and external emphysema. The external emphysema follows the cellular tissue and skin; the internal follows the bronchi and serous paths. Therapeusis consists in quieting respirations, rendering the patient insensible and evacuating the air by puncture with trocar.

Mediastinal emphysema as a complication of artificial pneumothorax occurred fifteen times in nine of sixty-three patients (Parfitt³⁹). There were symptoms of discomfort under the sternum and in the neck, and slight pain beneath the sternum and in the neck. Crackling noises on swallowing or on moving the jaws could be heard by the patients as well as through the stethoscope. Parfitt noted that all symptoms in his patients disappeared in thirty-six hours. It would not seem unlikely that some of the reactions noted during pneumothorax treatment and previously attributed to other causes are perhaps due to slight degrees of mediastinal emphysema. This would apparently be more likely to occur when air collects on the mediastinal side of the lung, when the mediastinum is unstable and when the intrapleural pressure becomes positive. In the majority of instances, the lung itself is injured. Pick⁴⁰ reported the occurrence of mediastinal emphysema in a patient receiving pneumothorax treatment which resulted from the rupture of a tuberculous cavity. Some relief was obtained by puncturing cutaneous blebs. The

37. Lenormant, C.: *Le traitement de l'emphysème médiastinal d'origine traumatique*, Presse méd. **28**:286 (April 8) 1911.

38. Ozanam, C.: *De la rupture pulmonaire chez les enfants et de l'emphysème général qui lui succède*, Arch. gén de méd. **1**:31, 1854.

39. Parfitt, C. D., and Crombie, D. W.: *Five Years Experience with Artificial Pneumothorax*, Am. Rev. Tuberc. **3**:385, 1919.

40. Pick, E.: *Ueber einen Fall von Haut und Mediastinalempysem bei Lungentuberkulose*, Wien. klin. Wchnschr. **38**:58 (May 7) 1925.

patient died two months later, and it is worthy of note that evidences of emphysema were demonstrable in the thickened pleura which was apparently not completely or solidly obliterated. Schill⁴¹ has shown that mediastinal adhesions may also be loosed during pneumothorax treatment. Serceer and Peicic⁴⁰ treated a patient suffering from mediastinal emphysema which developed following a tracheotomy by expressing air from the tissues. Cyanosis and dyspnea were relieved. In another case due to a ruptured tuberculous cavity, the condition failed to respond to similar treatment and to the introduction of a trocar over the jugulum. Jehn⁴² reported a case of mediastinal emphysema which followed fracture of the laryngeal box. Exposure of the jugulum, tracheotomy and the use of cardiac stimulants gave no relief. The patient died from a phlegmon of the mediastinum. Fracture of the thyroid cartilage and emphysema were also observed by Conwell.⁴³ Good results have apparently been obtained from the use of the Tiegel suction apparatus in some such instances of mediastinal emphysema. Wassermann⁴⁴ reported that mediastinal emphysema may simulate stenocardia, and Wiskovsky and Camrda⁴⁵ have reported the occurrence of mediastinal and subcutaneous emphysema in a patient after the inhalation of a bean into the right bronchus. Recovery occurred after the extraction of the foreign body through a bronchoscope.

Alexander and Follett⁴⁶ have discussed various types of emphysema. They made particular reference to that form which occurs in children and which is due to rupture of a congenitally or otherwise weakened alveolus. These authors have classified emphysema into three broad groups: (a) congenital, which is rare, (b) emphysema in infants due to a variety of causes which may be responsible for the rupturing of an alveolus, and (c) the traumatic group. Mediastinal and subcutaneous emphysema may be a consequence of congenital cystic lung (Box⁴⁷).

41. Schill, E.: *Pneumothorax Studien. Mediastinal Emphysem als Komplikation des kunstlichen Pneumothorax*, Beitr. z. Klin. d. Tuberk. **65**:505, 1927.

42. Jehn, W.: *Klinisches und experimentelles ueber das Mediastinal-emphysem*, Arch. f. klin. Chir. **38**:195, 1925; *Ein Beitrag zur Klinik und Pathologie des Mediastinal-emphysems*, Deutsche Ztschr. f. Chir. **140**:398, 1917; *Das Mediastinal-emphysem*, Ztschr. f. Chir. **48**:1619, 1921.

43. Conwell, H. E.: *Fracture of the Thyroid Cartilage*, J. Bone & Joint Surg. **11**:123 (Jan.) 1920.

44. Wassermann, S.: *Das Mediastinale Emphysem*, Wien. klin. Wchnschr. **6**:122, 1920.

45. Wiskovsky, B., and Camrda, I.: *Mediastinal and Subcutaneous Emphysema After Inhalation of a Bean into the Right Bronchus; Recovery After Extraction of a Foreign Body Through Peroral Bronchoscopy*, Bratisl. lekár. listy **11**:195, 1922-1923.

46. Alexander, M. E., and Follett, E. C.: *Subcutaneous Emphysema*, J. A. M. A. **72**:930 (March 29) 1919.

47. Box: *Bronchiectasis in Childhood with Some Observations on the Condition Known as Honeycomb Lung*, Lancet **1**:16, 1907.

Achard⁴⁸ was able to produce mediastinal emphysema in dogs by a variety of methods. He injected air subcutaneously over the thorax and elsewhere, and was able to produce mediastinal emphysema. We repeated this experiment in one instance (in a rabbit) and also obtained a positive result.

Generalized interstitial emphysema and spontaneous pneumothorax were observed as complications of bronchopneumonia following influenza by Berkley and Coffen⁴⁹ in 11 out of 1,701 instances. There were five deaths. This complication occurred in the more severely ill patients and often apparently followed a sudden severe paroxysm of coughing. The emphysema was first noted in the soft tissues of the episternal notch. All patients complained of choking sensations. Pneumothorax was observed twice.

Kelman⁵⁰ examined twenty patients who died of influenza, and at necropsy found marked vesicular and interstitial emphysema. The former was most marked, however, at the margins of the lungs. Interstitial emphysema involved mainly the anterior and posterior mediastina, which included the pericardium and pericardial fat. It could also be observed in the perirenal tissue. She produced experimental emphysema by inflating the lungs of dead rabbits with air by means of a bicycle pump.

Rapid and extensive emphysema with severe collapse caused by the passage of a cart wheel over the thorax, in which marked relief was obtained at once by multiple punctures of the skin, was reported by Bisshopp.⁵¹ Nine or ten punctures were made in the neck, back, cheek and dorsal region with a small knife, "and when the air rushed out it hissed and blew out the flame of a wax light." Emphysema of the scrotum was the last to disappear. Surgical emphysema, which resulted from a bayonet wound of the buttock which punctured the lung, was noted by Hayward.⁵²

Silvester⁵³ was of the opinion that the production of subcutaneous emphysema should prove an excellent means of saving the life of a

48. Achard, C.: Étude expérimentelle de l'emphysème du médiastin, *Bull. Acad. de méd.* **80**:609, 1918.

49. Berkley, Hugh K., and Coffen, T. Homer: Generalized Interstitial Emphysema and Spontaneous Pneumothorax as Complications of Bronchopneumonia, *J. A. M. A.* **72**:535 (Feb. 22) 1919.

50. Kelman, S. R.: Experimental Emphysema, *Arch. Int. Med.* **24**:332 (Sept.) 1919.

51. Bisshopp: Extensive Emphysema with Severe Collapse from Passage of a Cartwheel Over the Thorax Treated at Once with Marked Relief with Multiple Punctures of the Skin, *Brit. M. J.* **1**:163, 1884.

52. Hayward, J. D.: Bayonet Wound of Buttock: Lung Punctured; Surgical Emphysema, *Lancet*, August 11, p. 199.

53. Silvester, H. B.: On Life-Saving from Drowning by Self-Inflation, *Lancet* **1**:11 (Jan. 31) 1885.

person who has almost drowned. He has given an interesting account of the air chambers of certain birds and swim bladders of fish. He demonstrated how a body could actually be blown by forcing air under the skin of the wrist. For the average person he devised a simple method "which could be accomplished without the employment of any apparatus and in fact which might be performed without assistance in a moment, under the most adverse circumstances and by the most ignorant, if once instructed in it and without danger or pain, and suitable alike for the roughest sailor or the most delicate female." It was required that a sharp instrument be introduced opposite the first molar tooth and cheek down to the skin of the neck. On expiration, it would be possible to blow up the neck and chest to the nipples. In a communication to court, he wrote that in the absence of a sharp instrument the mucous membrane of the side of the mouth could be affected by the person's own teeth.

Entrance of air into the mediastinum during operations on the base of the neck has also been reported by Buford.⁵⁴ He has recorded two cases. One patient complained of extreme dyspnea, precordial fulness and pain and was quite cyanosed. Air hunger became great, and finally subcutaneous emphysema developed over the side of the neck and chest. Marked relief and improvement followed venesection.

That perineal emphysema may spread to the upper parts of the body was noted by Erichsen⁵⁵ who recorded its occurrence following puncture of the urinary bladder through the rectum for retention (see also Tatum).⁵⁶

The relationship of subcutaneous emphysema to abdominal operations has been discussed by Heil,⁵⁷ Madlener,⁵⁸ Meinert⁵⁹ and von Graefe.⁶⁰

54. Buford, Coleman G.: Entrance of Air into Mediastinum During Operations on Base of Neck, Surg. Gynec. Obst. **26**:540 (May) 1918.

55. Erichsen: Perineal Emphysema Spreading to the Upper Parts of the Body from Puncture of the Bladder Through the Rectum for Retention, Lancet **1**:89, 1860.

56. Tatum: Perineal Emphysema Spreading to the Upper Parts of the Body, Lancet **1**:90, 1860.

57. Heil, K.: Ueber die Entstehung des Hautemphysems nach Laparotomien, Arch. f. Gynak. **435**:52, 1896; Ein weiteren Beitrag zur Entstehung des Hautemphysems nach Laparotomien, Munchen med. Wchnschr. **35**:1208, 1900.

58. Madlener, M.: Das Haut Emphysem nach Laparotomien, Monatschr. f. Geburtsh. u. Gynak. **13**:305, 1901.

59. Meinert: Ueber emphysem der Bauchdecken nach Laparotomien, Zentralbl. f. Gynak. **50**:1328, 1895.

60. Von Graefe: Ueber locales traumatisches Hautemphysems nach Laparotomien, Munchen. med. Wchnschr. **42**:823 (Oct. 16) 1894.

In 1899, Klots⁶¹ reviewed the literature concerning subcutaneous emphysema of the mother which developed during childbirth. He collected forty instances. Thirty-one occurred in primiparas. Emphysema was first noted in the neck over the clavicle. It developed during the period of expulsion when the intra-abdominal pressure becomes markedly increased; the diaphragm immobilized and when attempts at forced inspiration were made with the glottis closed then emphysema interstitiale pulmonum must of necessity develop. Air will escape between the parenchyma of the lung and pleura to the anterior mediastinum. Klots noted that Decadas' patient had pleuritis, Eisler's had previously had hemoptysis and one patient (Filippow) eclampsia. Nearly all the women so affected were robust. The abnormal local conditions were too large a head, contracted pelves and rigidity of the soft parts. The prognosis in general was considered to be good and resorption rapid. No treatment was suggested. Klots stated that when subcutaneous emphysema develops labor should be ended. The condition, he feels, is frequently overlooked.

The relation of mediastinal and subcutaneous emphysema to pneumothorax has recently received consideration at the hands of Kovacs.⁶²

Le Soudier⁶³ has reported the association of subcutaneous emphysema with diphtheria. Three similar occurrences had apparently been previously reported.

Morgan,⁶⁴ in 1826, discussed the development of subcutaneous emphysema into the loose tissue of the eyelid which followed a fracture of the os frontale; the air came from the frontal sinuses. The principle involved is obviously the same throughout the body.

General emphysema may follow the rupture of a viscus. Such a case which followed rupture of the stomach has been described by Newman.⁶⁵

It is important, as von Braman⁶⁶ pointed out, to differentiate between an injury to the pleura costalis and the pleura pulmonalis. Subcutaneous emphysema which develops after an injury of the rib implies that the

61. Klots, S.: Emphysema subcutaneum während des geburctes Entstanden, *Ztschr. f. Geburtsh. u. Gynäk.* **41**:357, 1899.

62. Kovacs, F.: Ueber den Emphysempneumothorax, *Wien. klin. Wchnschr.*, vol. 21, p. 716.

63. Le Soudier: Un cas d'emphysème sous-cutane dans la diphtérie, *Arch. d. méd. d. enf.*, 1917, July, 20, p. 360.

64. Morgan: Fracture of the Os Frontis into the Frontal Sinus with Extravasation of Air into the Cellular Membrane of the Eyelid, *Lancet* **10**:31, 1826.

65. Newman: A Case of General Emphysema Following Rupture of the Stomach, *Lancet* **2**:728, 1868.

66. Von Braman: Ueber die Behandlung des nach Lungenverletzungen aufgetretenden allgemienner Korperemphysems, *Verhandl. d. deutsch. Gesellsch. f. Chir.*, 1893, p. 114.

pleura pulmonalis is injured—in other words, that there has been injury to the lung tissue. No matter how small, a pneumothorax must of necessity be present. Even a lateral view with the affected side up may, however, fail to disclose its presence. The lung, if it is injured when a rib is fractured, is usually injured during inspiration. Von Braman has treated such patients by closed drainage. Air which escapes into the thorax is thus expelled. In discussing von Braman's paper, König rightly pointed out that blood in many instances sears over the wound. The early development of pleural adhesions would act in the same way.

TREATMENT OF MEDIASTINAL AND SUBCUTANEOUS EMPHYSEMA

It would appear that the treatment of mediastinal emphysema must vary with the cause, severity and progress of the condition. If there is an associated tension pneumothorax or an increased intrapleural pressure, they should be relieved, the former, if necessary, by an open operation; the latter is done by use of the pneumothorax apparatus. If the mediastinal emphysema develops after strumectomy, a cold wet pack placed substernally may prevent the further entrance of air into the mediastinum. Teigel's suction cup or a needle placed in the jugulum and attached to a pneumothorax apparatus may be of help. Subcutaneous emphysema usually responds to incision. If cyanosis is extreme, venesection might be suggested. The patient should be kept quiet as cough may expel more air from the lung. Closed drainage might also be considered. Pain should be alleviated, as the splinting of the thorax may favor the progress of the condition.

SUMMARY

Experiences concerning some of the consequences of variations in mediastinal pressure have been here recorded.

Particular attention has been paid to mediastinal and subcutaneous emphysema.

Variations in the arterial, venous and intrapleural pressures and respirations which resulted from changes in the size, shape and contour of the anterior and posterior mediastina have been noted.

Practically all of the forty experiments were performed on rabbits, because the mediastina of rabbits are best fitted for such experiments.

Experiments with a rubber balloon in the mediastinum illustrated the effects of sudden confined increase in mediastinal pressure, and how these effects can be made to disappear by reducing the pressure. The consequences were local and varied directly with the extent to which the balloon had been inflated and the position which it occupied in the mediastinum.

The initial change in the blood pressure following the injection of air into the rubber balloon which was placed in the mediastinum was always a fall in blood pressure.

The anterior mediastinum was considered to lie in front of the root of the lung, the posterior mediastinum behind the root of the lung.

It is much easier for compression of the large blood vessels to occur than of the trachea or bronchi.

Some of the consequences of increased mediastinal pressure are pulmonary emphysema which may be partly hyperventilation or hypoventilation of the lungs, stagnation of blood in the lungs, hindered heart action, edema of the lungs and the development of fluid in the pericardial cavity.

Edema of the tracheobronchial mucous membrane may also be a consequence.

The position and size of the opening which is allowing air to escape into the mediastinum is of the same import as it has been shown to be in open pneumothorax by Graham. The presence of a tension pneumothorax or of an uncomplicated unilateral or bilateral pneumothorax as consequences of mediastinal emphysema must always be excluded.

Mediastinal emphysema was produced directly by various means, including the direct injection of air into the mediastinum and by producing tracheal fistulas.

The courses which air may take in the production of mediastinal and subcutaneous emphysema have been pointed out. In so doing the air follows with predilection the normal fascial planes, particularly the sheaths which surround blood vessels. It may also extend retroperitoneally, outline the kidneys and compress the renal vessels.

Large amounts of blood can become stagnant in the lung without producing marked pressure changes in the circulation.

The direct injection of frequent small amounts of air into the mediastinum caused a fall in blood pressure and an increase in respiratory rate. The blood pressure soon returned to normal if the injections were not repeated too frequently. Only gradual rises and falls in venous pressure were observed. These rises and falls in venous pressure followed no definite rule. Transitory terminal rises concomitant with the fall in arterial pressure could be observed.

The effects of the injection of mixtures of paraffin and iodized oil which solidified have also been recorded.

Some remarks concerning treatment of the condition have been made. With regard to the treatment, it can be said that the necessity of ruling out the presence of a tension pneumothorax or of a simple pneumothorax is of extreme importance.

9. COMPARISON OF IODIZED OIL AND BROMINIZED OIL*

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AND

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The use of a brominized oil as a contrast medium in roentgenology has been suggested in order to overcome certain dangers which are supposed to be inherent in iodized oils. Several manufacturers have made preparations of brominized oil and have put them out under various names. Our experience with this type of oil has been limited but sufficient to give us certain impressions.

In view of the fact that other investigators have made statements that iodized oil is likely to produce an aggravation of symptoms and signs in tuberculous patients, we thought it advisable to review our statistics to determine whether we could substantiate this. During the routine work in our chest service, 277 patients have received intratracheal injections of iodized oil (lipiodol). Thirty-five of these were cases of chronic pulmonary tuberculosis. Three patients, none of them tuberculous, developed definite symptoms and signs of iodism, but all of them had swallowed a considerable quantity of the oil which had been introduced. We have not observed any unusual after-effect in any of the tuberculous patients who were given injections. A few patients have been given injections with brominized oil, and none of these has shown any bad effects.

If one refers to Archibald and Brown's¹ article on "The Dangers of Introducing Iodized Oil into the Tracheo-Bronchial System," it will be noted that the iodized oil was injected into tuberculous patients through a bronchoscope or intratracheal catheter. When one considers that many tuberculous patients develop a rise in temperature, an increase in cough and other symptoms in addition to increased physical signs following muscular effort, it can readily be seen that the procedures which were used rather than the oil itself in many cases might explain the reaction.

In this clinic the method of aspiration described by one of us (J. J. S.²) has been employed. This method causes the patient a minimum of

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1. Archibald, E. W., and Brown, A. L.: Dangers of Introducing Iodized Oil into the Tracheobronchial System, *J. A. M. A.* **88**:1310 (April 23) 1927.

2. Singer, J. J.: A Simple Method of Introducing Iodized Oil into the Lungs, *J. A. M. A.* **87**:1298 (Oct. 16) 1926.

muscular exertion. We feel that this has been a factor accounting for the lack of bad effects from the administration of the oil.

Ballou³ has shown that the injection of iodized oil into the lung of a rabbit is not followed by any inflammatory reaction that can be demonstrated either macroscopically or microscopically. However, rabbits with pulmonary tuberculosis, made more acutely ill by various means, had their death hastened by the endobronchial injection of oil, not, however, because of an extension of the process but rather because of an aggravation or intensification of the underlying condition. So far as



Roentgenogram of the chest of a woman, aged 23, with bilateral bronchiectasis. By the aspiration method 20 cc. of iodized oil was first introduced into the right side; then the patient was caused to lean toward the left and 20 cc. of brominized oil was introduced into the left lung. It may be readily seen that the density of the bronchial outlines is much less on the left side where the brominized oil entered.

we know, similar experimental work has not been undertaken with a brominized oil. Putnam⁴ studied experimentally the irritating effect of brominized oil by introducing it into the anterior chamber of the eye.

3. Ballou, H. C.: *Lipiodal bei Lungentuberkulose: experimentelle Klinische und pathologische Studie*, Frankfurt. *Ztschr. f. Path.* **36**:207, 1928.

4. Putnam, Jackson: *Some Brominized Oils for Radiographic Use*, *J. A. M. A.* **87**:1102 (Oct. 2) 1926.

using the resulting increase in cell count of the vitreous humor as an index of the severity of the reaction. Dyroft,⁵ Rad⁶ and Iglauer⁷ have used a brominized oil clinically in the lungs, especially in cases of tuberculosis. Iglauer stated the belief that a brominized oil causes less reaction than iodized oil in pulmonary tuberculosis. However, his conclusions are based on two series of cases which we believe cannot be accurately enough compared.

Another factor to be considered in comparing iodized oil with brominized oil is the fact admitted by Iglauer, Rad and Dyroft that the density of a shadow cast by an oil containing bromine is less than that of an oil containing iodine. This, of course, is a characteristic which varies with the atomic weights of the elements. Since it is often desirable to outline structures within dense shadows cast by the x-rays, it is readily seen that it is advantageous to have a contrast medium which is as opaque as possible. The iodized oils have been satisfactory as a contrast medium.

It would be an advantage if the concentration of bromine could be made great enough in an oil of suitable viscosity so that it could be used in cases in which iodine is contraindicated.

Our experience with iodized oil in patients with pulmonary tuberculosis up to the present time does not contraindicate its further use in such conditions.

5. Dyroft, Rudolf: "Contrastol" ein neues Kontrastmittel für die Darstellung engkolibriger Hohlräume, *Deutsche med. Wchnschr.* **52**:397 (March 5) 1926.

6. Rad, Alexander: Die Füllung des Bronchialbaumes mit Jodolen und Bromipin, *Wien. klin. Wchnschr.* **39**:1011, 1926.

7. Iglauer, Samuel, and Kuhn, Hugh: Advantages of Brominized Oil in Bronchography in Tuberculous Patients, *J. A. M. A.* **90**:1278 (April 21) 1928.

10. EFFECTS OF PRESSURE ON THE HEART, WITH REFERENCE TO THE ADVISABILITY OF DECOMPRESSION OF GREATLY ENLARGED HEARTS

EXPERIMENTAL STUDY *

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This is an experimental study of the effects of pressure on the heart. Its purpose is to determine the feasibility of decompression of a massively hypertrophied heart in the human being. It would seem that in cases in which the heart is greatly enlarged, there might be an abnormally high pressure on the heart because it is encased in the non-yielding, bony thoracic cage. In considering this question, we desire to focus attention particularly on the question of the harm produced on the heart muscle by pressure exerted on it by the wall of the chest because of the massive enlargement of the organ. We are here not considering the questions of giving relief by decortication of a thickened pericardium (Delorme) or by allowing the heart to contract against a yielding instead of a rigid structure, as is proposed in the cardiolysis of Brauer in cases of chronic mediastinopericarditis. There are many cases of massive enlargement of the heart in which there are no clinical signs of an adhesive mediastinopericarditis and in which also decortication itself would not be indicated because the pericardium is neither thickened nor adherent.

The experiments were made on normal hearts of dogs and consisted of applying pressure continuously, for varying periods of time, to the ventricles, to the auricles or to both. Blood pressures were recorded from the femoral artery at the same time. The experiments recorded here are acute experiments, and the changes in blood pressure are those which occur soon after the external pressure on the heart is altered.

CLINICAL ASPECTS

Decompression of an enlarged heart was advocated by Alexander Morison,¹ of Edinburgh, in 1907 and was performed on a patient of

* From the Department of Surgery, Washington University School of Medicine and Barnes Hospital.

1. Morison, A.: On Thoracostomy in Heart Disease, *Lancet* 2:7 (July 4) 1908; Further Report on a Case of Thoracostomy for Heart Disease, *ibid.* 2:1494 (Nov. 20) 1909.

his by E. C. Stabb, with marked improvement. He recommended the removal of ribs, costal cartilages and a portion of the sternum for relief from embarrassment to the hypertrophied heart. He considered this for (1) the relief of increased intrathoracic pressure due to the large heart and (2) to prevent undue stimulation of the heart from continued thrusts or blows against the ribs. It seems to us that he might have added, also, that anemia of the heart muscle and interference with diastole would probably result from an increase in the extracardiac pressure.

Bewley² reported a case of decompression for hypertrophy of the heart in which sections of the third, fourth and fifth ribs were removed along with the lower half of the sternum. He gave the indication for such decompression as follows: "To sum up, when we find that the ribs or sternum, or both, are distinctly moved up by each systole of the heart, I hold that this movement may be looked upon as the heart's prayer for more room."

Lenormant and Merle D'Aubigne³ collected fourteen cases in which the operation for decompression of the enlarged heart had been carried out. Of these fourteen patients five, or 35 per cent, showed definite and lasting improvement. These authors considered such a percentage remarkable in view of the original condition of the patients on whom the operations had been carried out. It is not certain, however, that in all these cases the operation was performed merely for decompression. It seems more probable that in many cases the operation was indicated by the presence of a chronic adhesive mediastinopericarditis. Such cases do not properly fall within the group under consideration here.

PREVIOUS INVESTIGATIONS

Investigations have been made in which the normal pressure on the exterior of the heart has been altered. Most of these investigations in the past have been concerned with the changes incident to removal of the pericardium. It is thought that this produces a decrease in support and hence a decrease in the normal external pressure on the heart. Kuno⁴ found that opening of the pericardium causes a fall of venous pressure, a rise of arterial pressure and an increase of output. Beck and Moore⁵ found little change in the function of the heart in animals from which the pericardium had been removed.

2. Bewley, H. T.: A Clinical Lecture on Cardiolytic, *Brit. M. J.* **1**:915, 1910.

3. Lenormant, C., and D'Aubigne, R. M.: La thoracotomie précordiale dans les symphyses et certaines hypertrophies cardiaques, *J. de chir.* **31**:161, 1928.

4. Kuno, Y.: The Significance of the Pericardium, *J. Physiol.* **50**:1, 1915-1916.

5. Beck, C. S., and Moore, R. L.: The Significance of the Pericardium in Relation to Surgery of the Heart, *Arch. Surg.* **11**:550 (Oct.) 1925.

The changes in the circulation have been studied in normal animals in which the intrapericardial pressure has been raised above the normal. This increase was produced by the introduction of fluids and gases within the pericardium. Rose⁶ first termed this "tamponade."

In these tamponade experiments, marked changes in the circulation and in the respirations are noted. As the intrapericardial pressure was raised the systemic blood pressures fell, the pulmonary venous pressures rose and the respirations became deeper and slower.

EXPERIMENTAL WORK

We wish to point out that the present experiments with increased extracardiac pressures are not studies in heart tamponade. The present study is concerned with pressures applied directly to the ventricles or to the auricles. In tamponade experiments, equal pressures are applied simultaneously to the ventricles, to the auricles and to the thin-walled veins (the venae cavae and the pulmonary veins) entering the pericardium. The effects of tamponade due to fluids are mainly those incident to compression of these veins. It is probable that no such compression occurs in the veins entering the pericardium in cases of hypertrophy of the heart. It is logical to think that in these cases the increase in extracardiac pressure is most marked on the ventricles and auricles. Our experiments, therefore, more closely resemble the state of affairs in the hypertrophied human heart which is gripped within the bony thorax.

Method.—Normal adult dogs were used in these experiments. They were fully anesthetized with ether; the cavity of the left side of the chest was opened widely after artificial respiration had been instituted with the Erlanger-Gesell apparatus. Intermittent positive intratracheal pressure was obtained by this method. This closely resembles the normal respiratory cycle.

After the pericardium had been exposed, the femoral artery was exposed, a cannula was inserted and this attached to a mercury manometer or to the more sensitive Hürthle manometer. The changes in blood pressure were recorded on a drum of smoked, glazed paper.

The external pressure on the heart was increased above the normal by weights laid directly on the intact pericardium over the ventricles, by pressure applied to the ventricles or the auricles by the fingers or by interrupted sutures accurately placed in the intact pericardium in such a manner as to apply pressure to the ventricles or to the auricles when the sutures were tightened.

The animals were given a lethal amount of ether at the end of the experiment.

Analysis.—Figure 1 shows the effect of moderate compression of the central portion of the ventricles. In this instance, care was used to prevent the heart from slipping upward and thus compressing the pedicle of the heart.

6. Rose, E.: Herz Tamponade, Deutsche Ztschr. f. Chir. 20:329, 1884.



Fig. 1.—Changes in the systemic blood pressure during sustained pressure on the ventricles. There is a fall in blood pressure and a fall in the pulse pressure. The pulse pressure shows a tendency to approach the normal due to the compensatory activity of the arterial system. On sudden release of the pressure on the ventricles the diastolic pressure rises above the normal since the compensatory mechanism is not released suddenly. The pressure is applied at point A and released at point B.

The tracing shows the consequent changes in the pulse pressure and in the blood pressure within the femoral artery. Immediately on increase of the extracardiac pressure in the midportion of the ventricles at point *A*, there is a marked fall of the diastolic pressure, a more marked fall of the systolic pressure and, as a result, a lessening of the pulse pressure. Then follows a rather rapid rise in the systolic pressure. This is a manifestation of compensation in the circulatory system. The diastolic pressure remains low.

On release of the pressure on the ventricles at point *B*, the systolic pressure immediately rises above the normal. This, we believe, indicates the compensatory mechanism of the arterial system which aids in maintaining the normal blood pressure. When the heart is suddenly restored to normal conditions, this acting compensatory mechanism of the arterial system does not release itself so suddenly, and hence the diastolic pressure rises above the normal. The systolic pressure returns to normal, however, within a few minutes. There is a similar rise in the diastolic pressure, but the increase above the normal is not so great as with the systolic pressure. The pulse pressure is increased as a result of this inequality.

Figure 2 is a tracing made with the rather sensitive Hurtle manometer. It was made in the same fashion as was the tracing shown in figure 1. The upper pointer indicates the pulse pressure, the diastolic and the systolic pressure. The upstroke is due to systolic pressure. The parallel lines show the calibration for the manometer in millimeters of mercury. The time marked is in seconds.

Four interrupted stitches were placed in the intact pericardium in such manner that when they were tightened pressure was brought to bear on the ventricles of the heart. This was done, at point *A*, with results similar to those shown in the tracing in figure 1.

The second and third pronounced falls in the blood pressure, at points *B* and *C*, were produced by squeezing the ventricles tightly with the fingers with such marked compression that the pulse pressure falls very low, as do the diastolic and systolic pressures.

The fourth disturbance in the blood pressure, as shown on the tracing at point *D*, is due to marked compression of the auricles with the fingers. It shows disturbances in the systemic circulation similar to those produced by compression of the ventricles.

Figure 3 is a tracing made by the sluggish mercury manometer as it records the blood pressures in the femoral artery. It shows the comparative effects on the systemic pressure of hammering the ventricles with a hammer and sustained pressure on them produced by the fingers.

The first irregularities shown in the tracing between points *A* and *B* are due to extrasystoles induced by hammering the ventricles repeatedly with a hammer. Sharp, forceful blows were dealt the ventricles at inter-

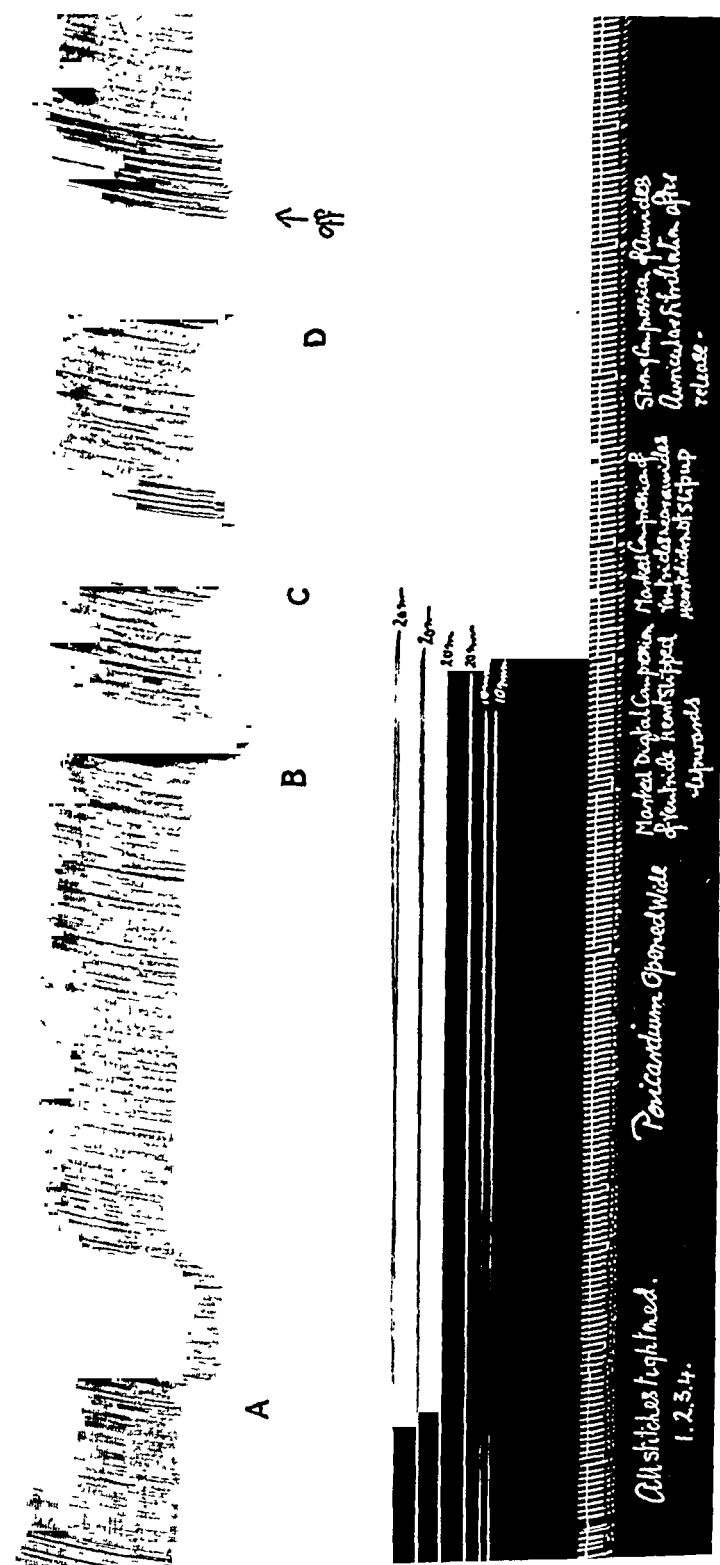


Fig. 2.—Result of moderate compression of the ventricles at point *A*. At point *B* the ventricles are strongly compressed with the fingers. The same marked compression was applied at point *C* and the auricles were compressed at point *D*.

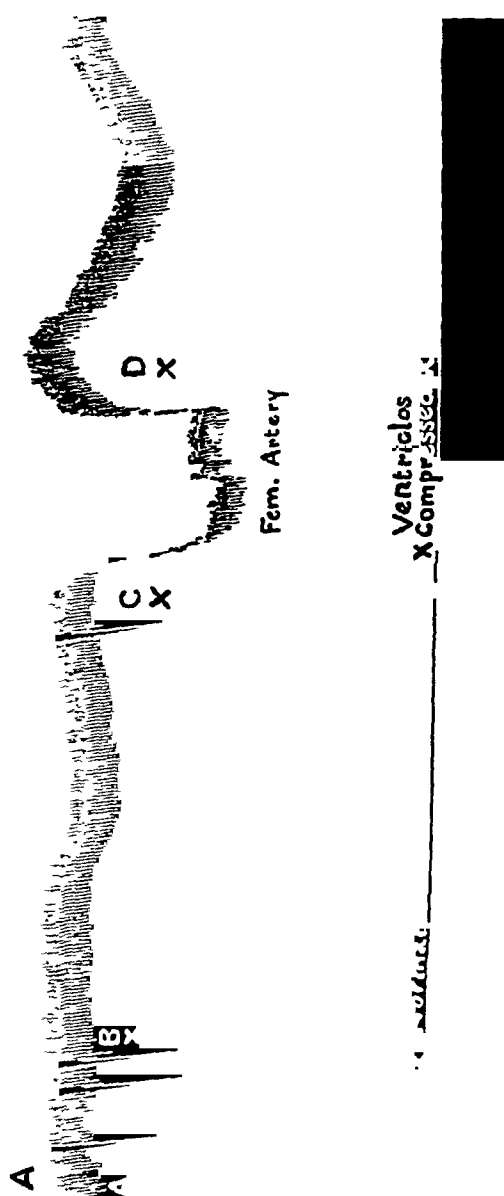


Fig. 3.—Section A-B shows the effect of hammering the ventricles with a hammer. The mean blood pressure is undisturbed, but there are numerous extrasystoles. Section B-C is the normal blood pressure. At C the ventricles were compressed, and at D the pressure was released. Sustained increased extracardiac pressure produces more marked changes in the blood pressure than nonsustained increased pressure.

vals not exceeding one per second nor less than one per two seconds. The tracing shows that the mean arterial pressure is unchanged by such procedures. The entire record is not shown in the figure here, but the terminal portion which is shown, is representative of the whole. Sometimes such hammering will set the ventricles into fibrillation. Unless this occurs, there seems to be but little effect on the mean arterial pressures in the systemic circulation.

The second disturbance shown in the tracing at point *C* is a marked fall in the mean pressure accompanied by a fall in the pulse pressure. This alarming fall in the systemic arterial pressure was occasioned by moderate compression of the ventricles with the fingers.

The tracing shows most clearly that a sustained increase of the extracardiac pressure applied to the ventricles produces a more marked fall in the mean blood pressure than repeated nonsustained increases.

This tracing indicates, therefore, that repeated thrusts of the enlarged human heart against the wall of the chest might be of little consequence. It also indicates that a heart which has become enlarged sufficiently to be impinged on continuously by the rigid thoracic wall might suffer impairment of its efficiency.

COMMENT

More than 100 observations were made on the hearts of 12 dogs. A careful analysis of the records shows that whenever the extracardiac pressure is increased, and maintained for a considerable period of time, there is a decrease in the efficiency of the heart. This is manifest by a fall in the mean blood pressure in the systemic circulation and a decrease in the pulse pressure.

This is soon compensated for, in the normal animals, by changes in the arterial system which are to maintain the normal blood pressures.

The heart remains embarrassed by the sustained increase in extracardiac pressure.

It is logical to infer, therefore, that the human heart is similarly less efficient when it is enlarged sufficiently to be pressed on continuously by the bony framework of the thorax. Decompression of such an enlarged heart should relieve the increased extracardiac pressure and would be expected to increase the efficiency of the heart.

Two patients with greatly enlarged and chronically decompensated hearts were operated on for the purpose of affording a decompression. In neither case was there any clinical evidence of an adhesive mediastinopericarditis. Both patients showed marked temporary improvement, but both ultimately succumbed. In one case, however, death was due not to the cardiac condition but to an acute pneumonia which occurred three months after the operation. Even during the pneumonia there

were no edema or other signs of cardiac decompensation. It is interesting also that in this case, in which the patient received the greater benefit, the pericardium was opened and found not to be thickened. Decortication, therefore, was not indicated. The beneficial result seems to have been due entirely to the decompression. These cases, together with the descriptions of the operations performed on them, have been reported elsewhere by one of us.⁷

7. Graham, E. A.: Decompression of the Heart, *Ann. Surg.* 90:817 (Nov.) 1929.

11. CYTOLOGY OF SEROUS EFFUSIONS, WITH SPECIAL REFERENCE TO TUMOR CELLS*

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ST. LOUIS

The study of the cellular structure of effusions is a valuable laboratory procedure. The most satisfactory method of study is that devised by Mandlebaum.¹ The fluid is placed in a large Erlenmeyer flask and allowed to stand over night in the icebox. The supernatant fluid is decanted and the sediment poured in a large 50 cc. centrifuge tube and centrifugated for at least twenty minutes at a moderate speed. The supernatant fluid is again decanted and the sediment hardened with a diluted solution of formaldehyde, U. S. P. (1:10) or Zenker's fluid for twenty-four hours. The fixed sediment is then treated as ordinary tissue by running through alcohols, embedding in paraffin and staining with hematoxylin eosin. The tissue is cut from above down so as to include all the cellular elements.

This report is based on the study of fifty effusions prepared by this method from serous fluids in cases of malignant, cardiac and tuberculous disease. Incidentally, the specific gravity was noted in all fluids.

MALIGNANT EFFUSIONS

There were twenty cases of malignant disease in this series proved by autopsy, biopsy or a palpable mass, with gross characteristics of a malignant tumor. Effusions from these cases were studied with particular reference to the presence or absence of tumor cells. Zemansky² pointed out that in his series studied by Mandlebaum's method 60 per cent of fifty-five cases of carcinoma showed tumor cells in the effusions. In this smaller series, 80 per cent of the effusions showed cells which were interpreted as being malignant. A positive diagnosis of tumor cells may be made with the highest degree of accuracy. A negative diagnosis does not, of course, rule out a malignant condition. Obviously, there must be contact between the tumor and the fluid before tumor cells are "shed."

Tumor cells, as has been pointed out by Zemansky and others, appear in two main forms: (a) fragments of tumor tissue often showing glandular or pseudoglandular arrangements or clumps of tumor cells, and (b) isolated tumor cells, the characteristics of which will be mentioned later.

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1. Mandlebaum, F. S.: Proc. New York Path. Soc., 1900, p. 178.

2. Zemansky, A. P.: Am. J. M. Sc. **175**:673, 1928.

The first type is easy to diagnose and predominated in this series (thirteen cases). The cell clumps stand out as large deep-staining cells amid various types of blood cells and mesothelial cells (fig. 1). Occasionally the tumor fragments may be seen almost exclusively at the bottom of the centrifugate.

It is in those cases in which individual tumor cells occur that one may have difficulty in making a diagnosis. There were three such cases. Criteria for diagnosis here are large atypical deep-staining cells,

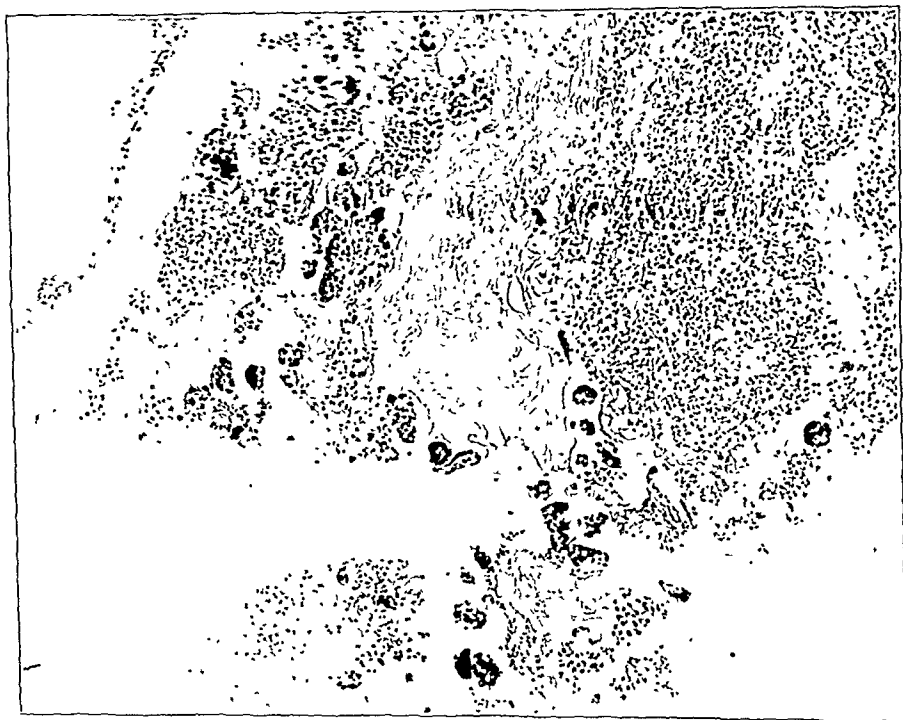


Fig. 1.—Pleural fluid from a case of adenocarcinoma of the ovary; low power magnification.

with a large eccentric nucleus or with several nuclei, sometimes showing mitotic figures, often vacuolated. Mesothelial cells which may or may not be clumped, occurring in transudates of long standing, are at times confusing. These must be carefully studied and differentiated by the criteria mentioned (fig. 2).

The cells often assume a glandular arrangement (eight cases) (fig. 3). The tumor cells may thus resemble the original tumor (fig. 4). In one case both pleural and peritoneal fluids were obtained, and both specimens showed the same type of cell.

A fluid may be positive at one examination and later appear negative. A patient with carcinoma of the pleura in whom the condition had metastasized from a bronchial carcinoma developed an effusion which on the first examination revealed many tumor cells. Two months later, a second tapping was done in which no tumor cells were found. It is possible that the fluid obtained from the second tapping came from an encysted effusion and not from the large pleural effusion. The

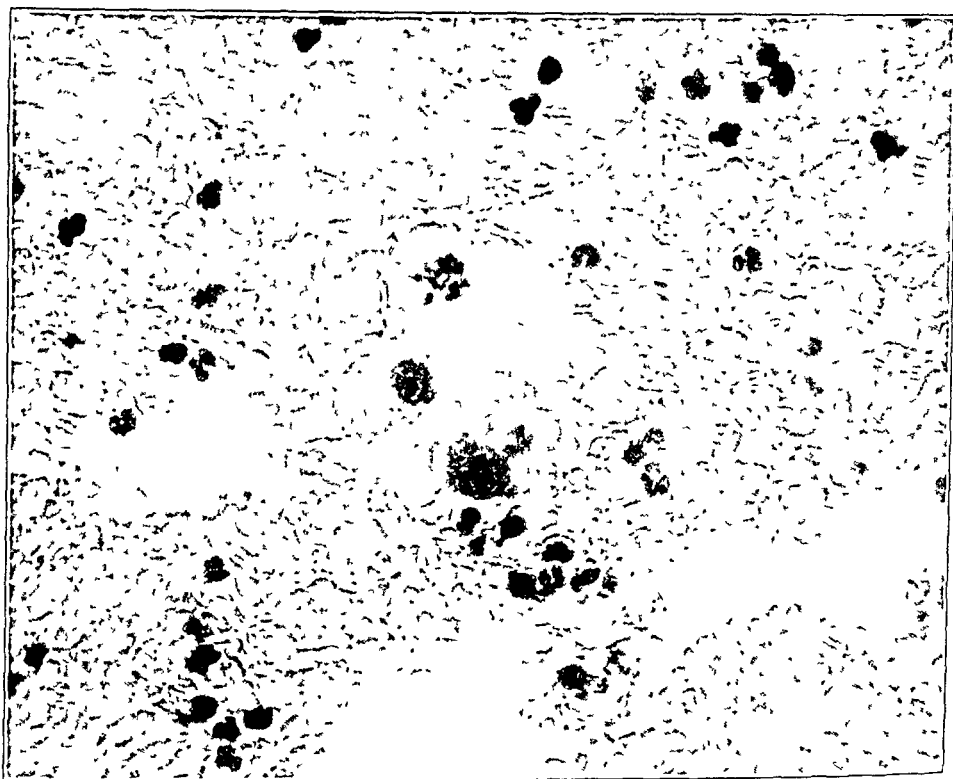


Fig. 2.—Pleural fluid from a case of metastatic carcinoma of the breast. Note the mitotic figure, high power magnification.

sputum in this case was treated by the same method and revealed no tumor cells.

Case 32 shows the necessity of careful search for tumor cells. While in the majority of cases cells are present in abundance, in this instance only one group of cells was found on which the diagnosis of malignant disease was made. A biopsy of a tumor of the neck revealed a metastatic carcinoma probably from the bronchus.

Tumor cells may appear in an effusion soon after the appearance of the fluid. In case 35 (autopsy confirmation), the patient developed

signs of pleural effusion while under observation. Tapping and study of the fluid a week after signs of fluid had developed showed numerous cancer cells. Figure 5 shows an adenocarcinoma in a pleural effusion which followed several months after removal of a breast for carcinoma in the male.

Four cases in which a positive diagnosis of tumor cells was made came to autopsy. All showed direct contact of cancer tissue with the

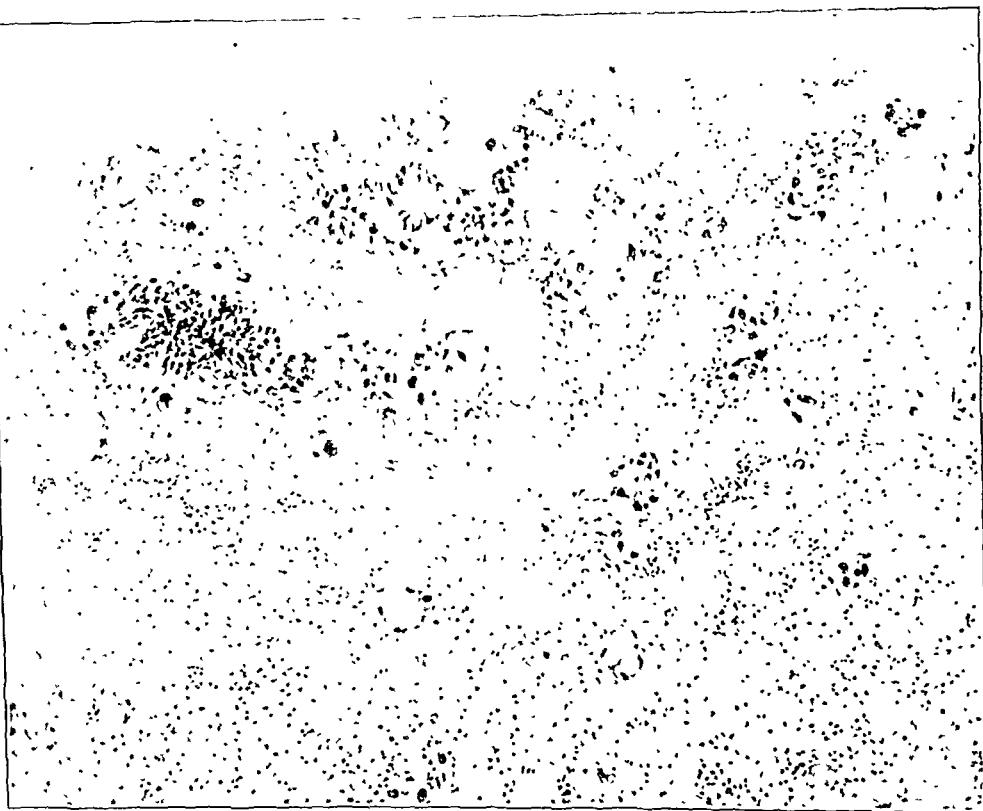


Fig. 3.—Pleural fluid from a case of adenocarcinoma of the bronchus. Note the alveolar arrangement; low power magnification.

effusions which had developed. Apparently this is essential before tumor cells are "shed" into the serous cavity.

The four negative examinations occurred in proved cases of carcinoma. Case 7 was one of carcinoma of the liver with metastatic glands in the retroperitoneal tissue. There was no actual contact of tumor and fluid. Case 28 was one of adenocarcinoma of the ovary with peritoneal involvement. Fluid in this case was obtained at operation and revealed a purely hemorrhagic fluid. Case 49 was one of carcinoma of the right bronchus and right lung combined with tuberculosis of

the base of the right lung. The fluid was small in amount and apparent only after pneumothorax. Autopsy showed a disappearance of fluid in the base of the right lung with replacement by fibrinous adhesions. The effusion could possibly have been due to an active tuberculosis of the base of the right lung, though there was also a tumor of the pleura. The fourth case was one of abdominal effusion in association with carcinoma of the liver, in which no postmortem examination was made.

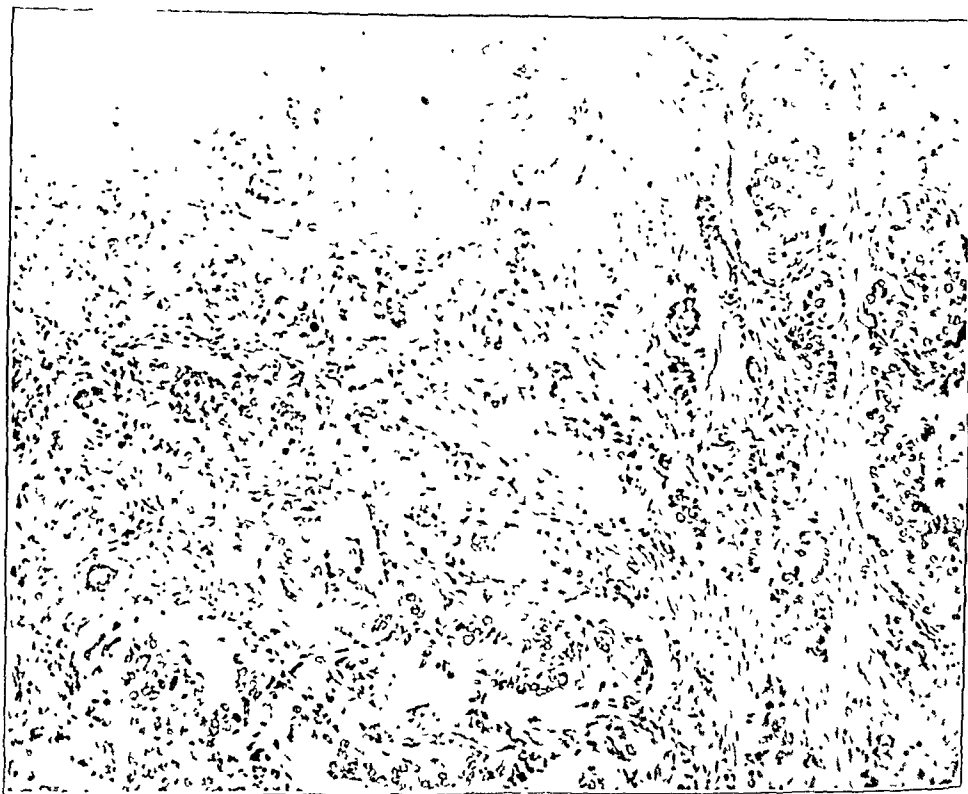


Fig. 4.—Section of gland of neck metastatic from adenocarcinoma of the bronchus in same case as in figure 3; low power magnification.

In none of the other examinations made could tumor cells be recognized as such, nor was a confirmed clinical diagnosis of cancer made in any of these cases. Whenever a carcinoma is in direct contact with the effusion that it has produced, one should expect to find malignant cells by the method described. There were no proved cases of sarcoma in the series studied. Zemansky has pointed out that a sarcoma is less likely to shed cells into its effusion than a carcinoma, owing to the more densely packed character of the sarcoma structure.

The appearance of the effusions varied from a clear straw-colored fluid as seen in transudates to turbid, bloody fluids. All specimens contained red blood cells in large amounts, more than in any other type of effusion. The specific gravity of the fluids ranged from 1.013 to 1.025; the average was 1.017. This figure is appreciably lower than that usually given in textbooks. There was no apparent relation between the specific gravity and the number of tumor cells present.

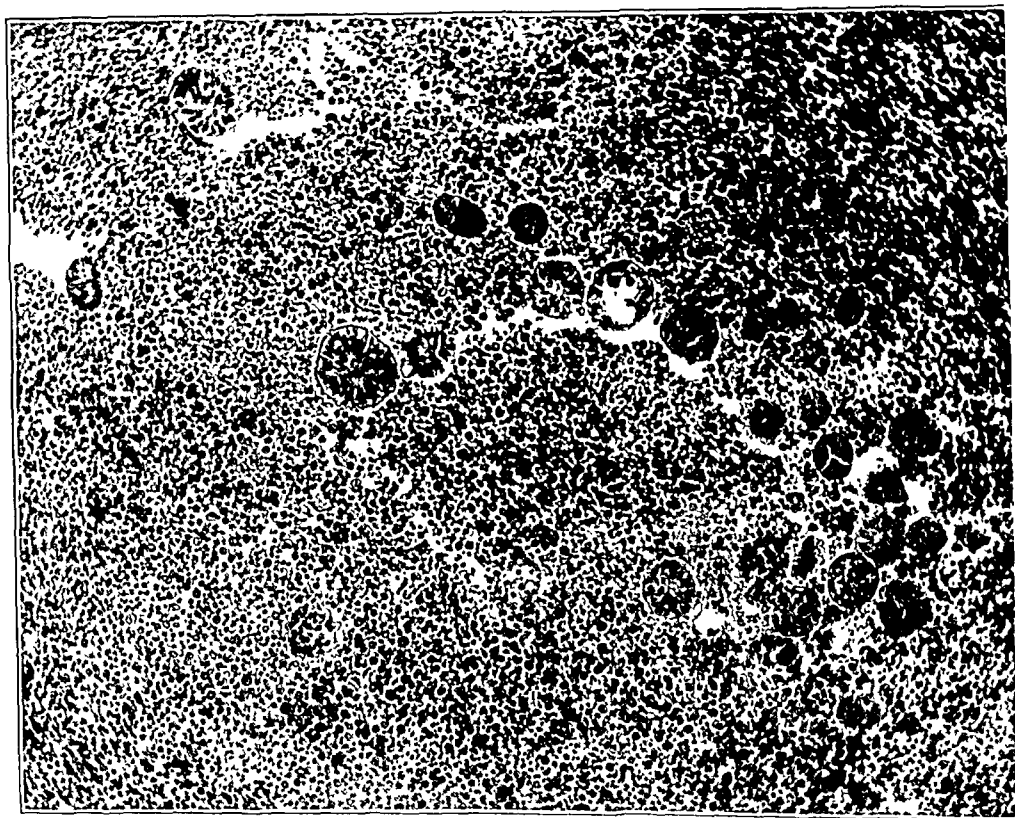


Fig. 5.—Pleural fluid from case of metastatic adenocarcinoma of the breast in the male. Note nests of tumor cells; low power magnification.

CARDIAC EFFUSIONS

There were ten cases of cardiac transudates, seven from the pleura and three from the peritoneum. All contained numerous red blood cells, less than in the cases of tumor and more than in the cases of tuberculosis. The predominating cell was the mesothelial cell, comprising more than 50 per cent of all the cells present. There were usually a few macrophages containing blood pigment, similar to the "heart failure" cell in the sputum in cardiac cases. The remaining

cells were chiefly lymphocytes and occasional polymorphonuclear neutrophils. The longer the effusion has been present, the greater the number of cells present. Clumped mesothelial cells may be mistaken for tumor cells. The former are usually smaller, more regular, have a single nucleus, show no mitosis, and do not stain so deeply as do the tumor cells. The specific gravity of these fluids varied from 1.008 to 1.014, with an average of 1.012.

TUBERCULOUS EFFUSIONS

There were twelve cases of tuberculosis in the series, ten from the pleura and two from the peritoneum. The predominating cell in nine specimens was the lymphocyte and in three the polymorphonuclear neutrophil. A few large mononuclears were usually present. In all cases red blood cells were present, but to a distinctly less extent than in tumor or cardiac effusions. The specific gravity ranged from 1.019 to 1.026; the average was 1.023. Eight of the sections were stained for tubercle bacilli, but none was found. This method, which theoretically should increase the possibilities of finding tubercle bacilli, is deserving of further study.

MISCELLANEOUS CASES

There were a number of miscellaneous cases with effusions which were studied. Two will be mentioned here. A pleural effusion in a case of Hodgkin's disease showed an equal mixture of lymphocytes and large mononuclear cells. There were about 10 per cent of cells containing elongated nuclei. A patient who had several large glands in the right side of the neck developed a right pleural effusion. Biopsy of a gland of the neck showed a chronic lymphadenitis, according to the pathologist. The effusion showed many large lymphocytic cells similar to the type of cell noted in the gland. This observation would suggest a lymphosarcoma. The patient is still under observation.

The urine from two patients with hypernephroma was studied, but no characteristic cells were found. Study of centrifugates prepared from urines is unsatisfactory.

CONCLUSIONS

1. Effusions resulting from carcinoma show "cancer cells" in a large majority of cases. These effusions show considerable blood. The specific gravity averages 1.017.

2. Cardiac transudates show a predominance of mesothelial cells. Red blood cells are abundant. The specific gravity averages 1.012.

3. Tuberculous effusions show a predominance of lymphocytes. Red blood cells are usually few. The specific gravity averages 1.023.

SURGICAL TREATMENT OF INTRATHORACIC TUMORS*

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The occurrence of intrathoracic new growths has been known for a great many years, but their recognition during life has been rare until comparatively recent years. The rapid advancement made in methods of thoracic diagnosis, especially since the use of the roentgen ray, has led to the early diagnosis of intrathoracic tumors and to the application of various types of treatment for the relief from symptoms. Roentgen rays and radium are probably the most commonly used agents in conservative treatment. In some of the cases of malignant tumors, such as the different types of malignant lymphomas and some of the sarcomas, there has been marked improvement. The lack of response of many of the tumors to the more conservative methods of treatment has stimulated surgical intervention with the view of radical removal of the diseased tissue.

I have previously reported five cases of intrathoracic tumors which were removed by transpleural operation. I am now reporting twelve additional cases, with a brief summary of the symptoms and methods of diagnosis and the surgical treatment. My purpose is to point out the difficulties encountered in many cases in establishing a definite clinical diagnosis of either benign or malignant tumors, to demonstrate the advisability of complete removal of benign tumors which may ultimately cause death from pressure on the surrounding organs, to show that the results of radical removal of malignant growths compare favorably with the results of surgical removal of malignant lesions elsewhere in the body and to emphasize the importance of early surgical intervention before the malignant growths have advanced beyond the possibility of surgical removal, and in the case of benign tumors, before they have caused serious injury to surrounding organs due to pressure or before they have undergone malignant change.

SIGNS AND SYMPTOMS

There are no characteristic signs by which early malignant intrathoracic tumors can be distinguished from benign intrathoracic tumors. The general condition of the patient is a great aid in establishing a diagnosis when this is correlated with the more special types of examination.

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The symptoms depend on the situation and the size of the tumor. They may be divided into two groups: those due to pressure or infiltration into the surrounding structures, and those due to inflammatory reaction in the tumor itself. The most common initial symptom is pain, which usually is in the wall of the chest at the site of the tumor, and which may be referred to different parts of the chest or arm, depending on the site of the tumor. In this group of cases, the initial symptom in fourteen cases was pain varying from two months to twenty-four years in duration. The pain was intermittent at the onset and often was precipitated by some inflammatory condition of the lungs, such as a severe cold or pneumonia, or often by extreme exertion. The pain in such cases is usually progressive, gradually becoming more or less constant. It is the usual symptom for which the patient seeks relief. The significance of this cannot be overestimated, as in several of the cases here reported the patients complained of pain in the chest for a long time before a thorough examination was made. In one instance, the patient had complained of pain in the upper right part of the thorax, that radiated down the arm, for more than twenty-four years. The first roentgenogram of the thorax was taken four years before admission, and the presence of a tumor was noted in the upper right part of the thorax. When this tumor was removed at operation it was found to have undergone malignant degeneration. It does not seem logical to assume that this tumor was malignant at the onset.

Dyspnea on exertion was noted in eleven cases; usually this is not noted on normal respiration, unless the tumor is enormous or if there is an associated pleural effusion. In three of the cases, there was a Horner syndrome, caused by pressure on the inferior cervical sympathetic ganglion. In all of these cases the tumor was malignant. Coughing and expectoration are not significant symptoms and are usually noted only when there is some irritation of the diaphragm or in dermoid tumors connected with or closely adherent to one of the main bronchi. Loss of weight is commonly noted in cases of malignant tumor and is often helpful in differentiating benign and malignant lesions, but at times it is noted also in benign lesions.

GENERAL EXAMINATION

Bulging of the wall of the chest was noted in five cases. In three of these cases there had been a history of previous injury; however, it is questionable whether the injury had any bearing as an etiologic factor. In twelve cases palpable tumor was not demonstrable. *Pleural effusion* may be present in either benign or malignant tumor but is more commonly associated with a malignant growth.

METHODS OF DIAGNOSIS

The physical examination is valuable in determining the general condition of the patient and is often of great aid in the differential diagnosis. It is of greatest aid, and often the deciding factor, in determining the advisability of surgical intervention.

The roentgen ray undoubtedly is the most valuable single method of diagnosis, and the importance of a thorough roentgenographic examination of patients who present suggestive symptoms cannot be overestimated. The single roentgenogram is useful in determining the presence of an intrathoracic tumor, and it affords definite knowledge as to its lateral and vertical position in the thorax. The lateral roentgenogram is of value in determining its position relative to the vertical and antero-posterior axes of the thorax and its relation to the anterior and posterior thoracic wall. The stereoscopic roentgenogram furnishes more definite knowledge as to the relation of the tumor to the normal structures within the thorax.

Artificial pneumothorax, when it can be employed in the absence of adhesions, is of great value in determining the relation of the tumor to the lung. In those cases in which the tumor is situated outside of the lung the introduction of oxygen gas in the pleural cavity will collapse the lung, and the tumor can be more distinctly visualized by roentgenographic methods. If the tumor is within the lung or if it is an anterior mediastinal tumor to which the median surface of the lung is adherent, the peripheral pulmonary tissue will collapse over the tumor. The posterior mediastinal tumors are usually not firmly attached to the parenchyma of the lung which will collapse away from the tumor readily on the introduction of oxygen. This method is of greatest benefit as an aid in distinguishing between intrapulmonary and extrapulmonary lesions.

Injection of iodized poppy seed oil 40 per cent within the bronchial tree often is of value in distinguishing between intrapulmonary and extrapulmonary lesions. Bronchoscopy has been a valuable addition to the diagnostic armamentarium. The presence of tumors outside of the lung, which cause pressure on the bronchi, often is suggested by signs of narrowing of the bronchi. This method is most useful in differential diagnosis, as in many instances of intrabronchial disease the diagnosis can be definitely established.

SURGICAL TREATMENT

The chief problems associated with the surgical removal of intrathoracic tumors are the difficulty of access through the bony incasement of the thorax and the danger of causing open pneumothorax with pulmonary collapse and mediastinal flutter.

The surgical approach depends, to some extent, on the site and type of tumor. If the tumor is attached to the lateral thoracic wall, I prefer to make the incision in that part of the wall of the chest which lies over the tumor; the site is determined by study of stereoscopic roentgenograms. If the tumor is in the anterior or posterior mediastinum, I prefer posterior thoracotomy, varying in vertical direction with the site of the tumor.

In several cases I have attempted extrapleural removal of posterior mediastinal tumors but always have found the pleura so adherent to the tumor that the pleural cavity was opened during its removal. This results in a condition of open pneumothorax, complicated by wide separation of the layers of the pleura, which delays healing; moreover, there is greater possibility of extensive pleural effusion. In one case the operation was performed in two stages. In the first stage an attempt was made to wall off the pleural cavity, but this failed because of pleural effusion which followed the first stage. In sixteen cases a transpleural operation was done in one stage. As no two cases are alike, the detail of the technical problem differs in each. This is given in the report of each case that is to follow.

The danger of open pneumothorax, with pulmonary collapse and mediastinal flutter, has been overcome by the use of intratracheal anesthesia induced by means of apparatus by which anesthetic gas and oxygen are administered under positive pressure. Ethylene or acetylene gas was used in all cases. The proper administration of the anesthetic should be in the hands of a skilled anesthetist. In cases in which partial collapse of the lung is required, the lung should be permitted to expand fully every four to five minutes during the operation. A suction pump should be applied to the intratracheal catheter before it is withdrawn to remove any mucus which may have accumulated in the trachea.

The after-care is important in these cases. All patients are given, intravenously, physiologic solution of sodium chloride or of dextrose. If there has been a fall of from 20 to 30 mm. of mercury in the blood pressure, a blood transfusion is given.

Postoperative pleural effusion occurs in practically all cases. In some cases aspiration will be required to relieve respiratory embarrassment, and if such embarrassment is not present, it will not be required, as the effusion will absorb rapidly. In many cases there is considerable hemorrhage, and in these cases, closed intercostal drainage should be instituted at the time of operation, and the tube should be removed at the end of from twenty-four to seventy-eight hours. Empyema is not uncommon after removal of infected dermoid cysts or in cases in which there has been injury to the pulmonary tissue. In these cases the patients are best treated by the closed method of intercostal drainage.

and in some cases resection of a rib may be required later. Patients with marked pulmonary collapse, dyspnea and cyanosis are best treated by being placed in an oxygen chamber; it often proves to be a life-saving procedure.

In nine cases in the group to be reported the tumor was benign and was completely removed by a transpleural one-stage operation. There were no deaths in this group. All of the patients have been completely relieved from symptoms, and a complete cure is to be expected. In this group of nine cases there was one case of osteochondroma, three cases of anterior mediastinal teratoma, three of posterior mediastinal neurofibroma, and two of cellular fibroma. In one of the cases of cellular fibroma, the growth originated in the upper posterior mediastinum, and in one, in the lower posterior mediastinum. In this group, it was not possible to make a definite clinical diagnosis of either a benign or a malignant lesion, and in several instances the clinical evidence was suggestive of a malignant condition. In one case bloody fluid had been aspirated from the chest on several occasions. I believe this group exemplifies the importance of exploration in all cases in which the diagnosis cannot definitely be established, and there is reason to believe, from the examination, that the tumor can be removed.

As would be expected, the results in cases of malignant tumors are not so satisfactory as in benign tumors. Of this series of seventeen cases, eight lesions proved to be malignant at the time of operation. In two of these cases the lesion was so extensive that only partial removal was possible. In six cases the tumor was removed completely. The results of operation in these eight cases are as follows:

Two patients are now living without evidence of recurrence, one patient three years and nine months after operation. The lesion in this case was an osteogenic fibrosarcoma originating on the wall of the chest; this was the only case in which a two-stage operation was performed. The other patient is living one year and seven months following operation. The growth in this case was a huge malignant endothelioma involving the entire lower part of the wall of the chest and diaphragm, necessitating resection of the portion of the diaphragm with the involved wall and closure of the opening with the relaxed diaphragm following the cutting of the phrenic nerve. I have heard from both of these patients recently, and they are doing their usual work.

The remaining six patients have died since operation, one patient of recurrence two years and two months after operation and after freedom from symptoms for a year and a half. The growth in this case was a fibrosarcoma and was known to have been present four years before operation; probably it was a benign fibroma at the onset. Four patients were benefited only slightly, if any, from the operation; in two of these

cases the growth was so extensive that exploration only was done, and in the remaining two cases the tumor was removed. These four patients died from recurrence within the first six months following the operation. The remaining patient, who had a teratoma which had undergone malignant degeneration to squamous cell epithelioma graded 4, died seven days following operation from cerebral hemorrhage; this was the only operative death in the series. The result in this group of malignant cases is not satisfactory, but it is at least encouraging in that a third of the patients were markedly benefited by the operation, and the results, I believe, compare favorably with those of highly malignant lesions elsewhere in the body. It exemplifies the importance of early diagnosis and early surgical intervention before the disease has progressed beyond the limit of radical excision.

Following is a summary of the history, results of general examination, methods of diagnosis, type of operation and the subsequent course in the twelve cases in which operation was performed and which have not been reported previously.

REPORT OF CASES

CASE 1.—A man, aged 56, was admitted to the Mayo Clinic on Jan. 23, 1928. The final diagnosis was intrathoracic osteochondroma, of the upper left anterior portion of the thorax. The chief complaint was pain in the upper left part of the chest of twenty months' duration. The patient had not had symptoms until twenty months before examination, when dull, aching pain in the upper anterior left portion of the chest had developed. The pain had been present more or less at night and frequently had kept him awake. For several days at a time he would have periods of freedom from the pain. It had radiated to the back, and down the left arm, and had become more constant, with various intervals of relief, but had remained of about the same degree of severity. About three months after the onset of pain, the patient noticed a tumor in the left upper part of the wall of the chest, just below the inner margin of the clavicle, which gradually had increased in size until it was about 5 cm. in diameter. Symptoms had not been severe enough to cause him to stop work. He did not cough or expectorate. There had been moderate dyspnea on exertion. Loss of weight had not been noted. Roentgenographic examination of the thorax, five years before admission, had disclosed evidence of a calcified area in the upper left part of the chest. There was no history of injury to the wall of the chest.

General examination gave negative results except for the presence of a fixed tumor just below the clavicle, on the left side, about 5 cm. in diameter. There was marked impairment on percussion, extending well beyond the limits of the palpable tumor. Moderate interference with transmission of breath sounds was noted. The hemoglobin was 76 per cent and the leukocytes, 8,000 per cubic millimeter. The Wassermann reaction of the blood was negative. Roentgenograms of the thorax revealed evidence of a dense, calcified area in the anterior part of the upper lobe of the left lung. Apparently it was chondroma of the cartilaginous ends of the second and third ribs, extending into the cavity of the chest.

Anterior thoracotomy, with resection of half of the second and third ribs and intercostal muscle, was performed on Feb. 24, 1928. Transpleural removal of the

intrathoracic portion of the tumor was effected. The thoracic cavity was closed without drainage. Intratracheal ethylene anesthesia was used. The incision was made parallel with the clavicle; the pectoralis major was split and the pectoralis minor muscle was pushed aside. A soft, cystic tumor was found protruding from the second interspace and also in the midaxillary line from the third interspace. Apparently it arose from the juncture of the cartilage with the second rib, posteriorly. The pleura was firmly attached to the tumor and could not be separated from it. The entire tumor, with the pleura, intercostal muscles, and portions of the second and third ribs was removed. The lung was adherent to the tumor and had to be separated for a distance of about 5 cm. (fig. 1 *A*).

The operative diagnosis was large intrathoracic osteochondroma on the left side, 11 by 9 by 5 cm, arising from the cartilaginous juncture of the second rib posteriorly and extending into the cavity of the chest, causing partial collapse of



Fig. 1 (case 1).—*A*, roentgenogram taken at time of patient's admission showing dense calcified area in the anterior part of the left upper lobe, apparently chondroma of the cartilaginous ends of the second and third ribs extending into the cavity of the chest; *B*, roentgenogram taken fourteen months after transpleural removal of intrathoracic tumor with partial resection of the second and third ribs anteriorly and the ninth rib posteriorly. The area of decreased density in the upper portion of the left side of the thorax is due to removal of the wall of the chest. The left lung is fully reexpanded. There is no evidence of recurrence of tumor (osteochondroma).

the upper lobe of the left lung. The pathologic diagnosis was osteochondroma (fig. 1 *B*).

There was considerable shock following operation. On the second day, the pulse rate was 130 beats per minute and the temperature, 101 F. Moderate cyanosis was noted. This gradually became more marked and the patient was placed in the oxygen chamber on the sixth day. Following this he improved considerably and the cyanosis lessened. The left thoracic cavity was aspirated on the seventh day, and 750 cc. of bloody fluid was removed. This was repeated

on the eleventh and fourteenth days, and culture of the fluid showed a gram-positive coccus to be present. On the sixteenth day, the left thoracic cavity was drained by intercostal drainage after resection of about 2.5 cm. of the ninth rib in the posterior axillary line. The thoracic cavity was irrigated with a surgical solution of chlorinated soda (Dakin's solution), and the patient's condition improved progressively. The empyema cavity gradually became obliterated, and the patient was dismissed on the sixty-third day after operation, with the lung completely expanded and the wound entirely healed. The final result has been satisfactory. Six months after the removal of the tumor the patient returned for observation and was in excellent general condition (fig. 2).



Fig. 2 (case 1).—Scar of anterior thoracotomy fourteen months after transpleural removal of intrathoracic tumor. There is some retraction of the anterior wall of the chest which bulges on coughing. The patient's general condition is good; he has gained 40 pounds and has complete relief from symptoms

It is of interest in this case that five years previously roentgenograms of the thorax disclosed a calcified area in the upper left part of the thorax and that symptoms were not noted until nearly three years later. There was no palpable tumor during this time, and the slight bulging was not noted until three months after the onset of pain. The pain was more or less constant after its onset. The reflex pain, radiating down the arm, is not uncommon in lesions of the upper part of the thorax. The good general condition of the patient, was clinical evidence that the

tumor was benign. Because of the apparent involvement of the second rib, the anterior surgical approach was used, which would permit removing the entire wall of the chest with the tumor. The necessity of removing such a large area of the wall of the chest with the tumor with only pectoral muscle, subcutaneous tissue and skin to close the thoracic cavity, resulted in collapse of the lung and an associated bloody pleural effusion which was aspirated on several occasions.

The oxygen chamber is of great benefit in cases in which there is marked pulmonary collapse. The patient should be given oxygen until there has been some reexpansion of the lung. However, I believe it is advisable to remove the patient from the oxygen chamber as soon as the condition will permit.

The empyema, in this case, probably resulted from a slight infection of the wound, as the fluid removed from the first aspirations was negative to culture. However, the empyema may have been the result of the repeated aspirations necessary for removal of the pleural effusion.

CASE 2.—A married woman, aged 31, was admitted to the clinic on July 16, 1928. The final diagnosis was left posterior mediastinal teratoma. The chief complaint was pain in the left arm and headache. There were multiple general complaints, such as migraine and constipation. She had had an indefinite pain in the left shoulder and arm more or less constantly for the year and a half previous to admission. She had had influenza six months before admission and since then the symptoms had been more marked. Considerable dyspnea on exertion had been noted. Her daily temperature had been from 99 to 100 F. Cough or expectoration had not been present. There had been some soreness of the left part of the chest, which had been more marked when she was lying down and which always had been present when she raised the left arm. Loss of weight had not been noted.

Results of general examination were essentially negative. The hemoglobin was 76 per cent and the leukocytes numbered 6,600 per cubic millimeter. The Wassermann reaction of the blood was negative. Roentgenographic examination of the thorax revealed in the posterior mediastinum, behind the heart, the shadow of a mass that apparently was attached to the spinal column, and was probably the shadow of a malignant tumor. Fluoroscopic examination showed a nonpulsile tumor (fig. 3).

On Oct. 10, 1928, left lower posterior thoracotomy was done, with removal of 12 cm. of the eighth rib and section of the seventh and ninth ribs at the costo-vertebral angle. Transpleural complete removal of the tumor was effected. Intratracheal ethylene anesthesia was used. The thoracic cavity was closed without drainage.

There was an irregular cystic tumor, arising, apparently, from the eighth intercostal space posteriorly and 5 cm. lateral to the thoracic aorta. It seemed to arise behind the pleura and had a broad elliptical attachment to the pleura. The tumor was adherent to the lower lobe of the right lung and also along the interlobar fissure between the lower and middle lobes. The adhesions were separated, and the tumor was found to arise from the posterior mediastinum, close to the thoracic aorta (fig. 4).

The operative diagnosis was of left posterior mediastinal teratoma, measuring 15 by 10 by 5 cm., attached to the thoracic wall, behind the pleura, at the eighth interspace posteriorly.

Pathologic examination revealed a cystic tumor lined with columnar epithelium, the wall of which contained cartilage and mucous glands. Probably it was part of the bronchial tree that had failed to develop. The tumor was filled with degenerated, cellular debris and mucus.

Convalescence was uneventful. The patient had little reaction from the operation. The pulse rate was 110 and the temperature was 100 F. on the second day. The temperature dropped to normal and the pulse rate to 70 on the sixth day and remained there throughout the remainder of convalescence. Dismissal from the hospital was on the twenty-second day, with the wound entirely healed. A roent-

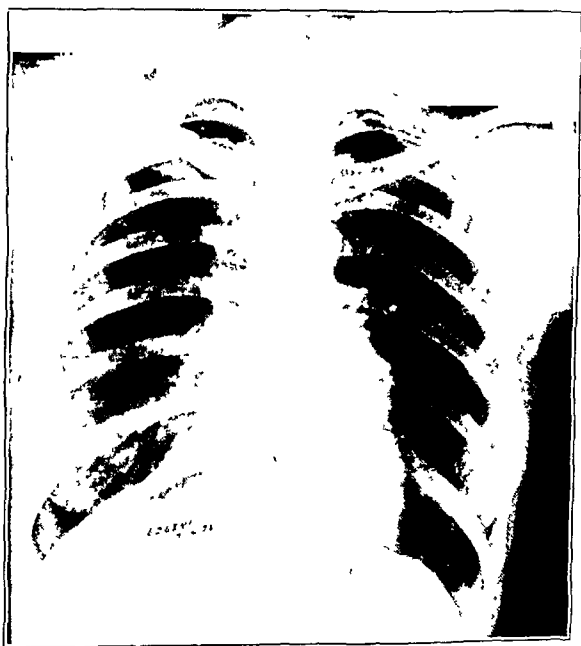


Fig. 3 (case 2).—Roentgenogram taken at time of patient's admission. The shadow extended from the posterior mediastinum posterior to the shadow of the heart in the left side of the chest at the level of the seventh and ninth ribs. The smooth outline suggests benign tumor.

genogram of the thorax at this time was negative. The subsequent course has been satisfactory. In a letter received April 12, 1929, the patient stated that her general condition has improved greatly and she has gained 14 pounds (64 Kg.) in weight. She still has many general symptoms, none of which is referable to the tumor.

It is questionable how much bearing the presence of the tumor had on the many general complaints of this patient, but it seems probable that the pain in the left shoulder and arm was the result of the tumor, espe-

cially since the symptoms were augmented by influenza. The roentgenograms of the thorax were difficult to interpret because of the position of the tumor behind the shadow of the heart. The somewhat infiltrating character of the margin of the tumor suggested that it might be malignant. However, the general condition of the patient did not indicate a malignant lesion. The tumor was readily exposed by posterior thoracotomy after the lung had been retracted forward. The lack of

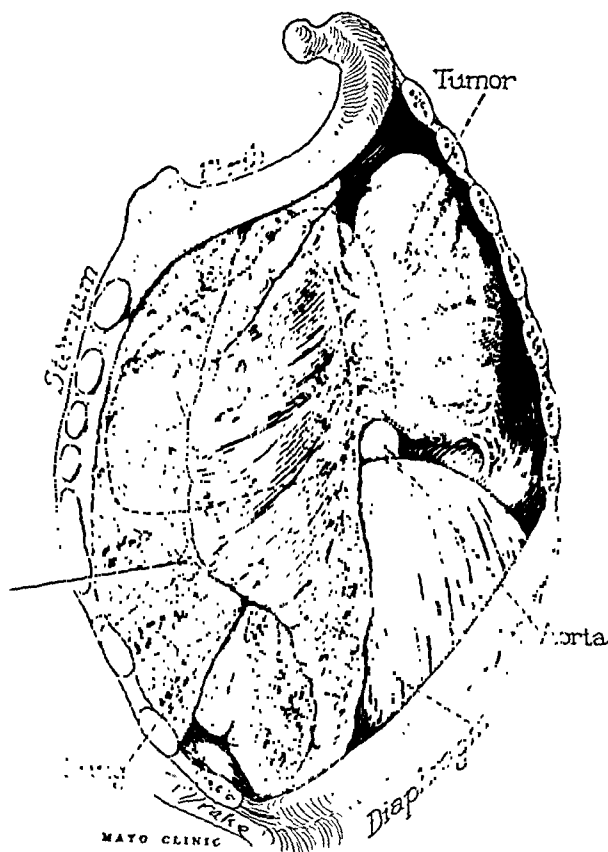


Fig. 4 (case 2).—The site of the left posterior mediastinal teratoma adherent to the hilum of the left lung, aorta and wall of the chest, posteriorly.

complications, postoperatively, is rather unusual considering the amount of adhesion between the lung and the wall of the chest which it was necessary to separate. Slight pleural effusion developed. However, it did not occasion any respiratory embarrassment; the fluid was not aspirated and was rapidly absorbed. The roentgenogram taken at the time of dismissal showed the lungs and pleura to be normal, with full expansion of the lung.

CASE 3.—A married woman, aged 48, was admitted to the clinic on Feb. 8, 1929. The final diagnosis was intrathoracic teratoma (dermoid cyst) of the anterior and superior mediastinum projecting slightly more into the left than into the right side of the thoracic cavity. The chief complaint was of pain in the left anterior part of the chest and in the back, of fifteen months' duration. Her present symptoms had begun fifteen months before admission, at which time she had been ill for about a week, without fever, but with much pain in the left anterior part of the chest, above the heart. This had been diagnosed as pleurisy. The pain had been made worse by coughing, sneezing, breathing deeply and by pressure on the anterior, upper left portion of the wall of the chest. The patient had been unable to lie on the left side and in attempting to do so, she had become dyspneic and had been obliged to sit up. The first attack had lasted about a week and the pain gradually had subsided but never had disappeared entirely. She had had repeated attacks of this type, which had come on without any known cause, and in the more recent attacks, a choking sensation, associated with the pain, had developed. These attacks gradually had been getting more frequent and severe, until shortly before admission they had been almost constant. The pain had remained in the same situation, had radiated through the chest, into the back, and had been made worse by any exertion. Cough, abnormal sputum or hemorrhage were not present. The patient gradually had been losing weight and strength, and at the time of admission had been unable to do her work. The attacks had been so frequent and severe at night that she had been restless and unable to sleep.

The patient looked tired. She had lost 11 pounds (5 Kg.) in weight during the six months previous to admission. There was slight prominence of the second rib, just to the left of the sternum. Examination of the thorax revealed in the upper part of the mediastinum an area of dullness 11 cm. wide anteriorly and 14 cm. wide posteriorly. Urinalysis was essentially negative. The hemoglobin was 73 per cent and the leukocytes numbered 13,100. The Wassermann reaction of the blood was negative. Roentgenograms of the thorax revealed evidence of a tumor in the upper left part of the mediastinum, anteriorly, which probably was benign. The fluoroscopic examination showed that the tumor was nonpulsile and in the anterior mediastinum; the lateral view showed the posterior mediastinum to be clear, with a rounded tumor in the anterior mediastinum (fig. 5).

Left posterior thoracotomy was done on Feb. 16, 1929, with resection of the seventh and section of the eighth, sixth, fifth and fourth ribs and intercostal muscles. Transpleural complete removal of the anterior mediastinal tumor was effected. The thoracic cavity was completely closed without drainage (fig. 6).

Approach was through a posterolateral incision, made at the level of the seventh rib; the greater portion of the seventh rib was removed. After the ribs had been cut above and below, the pleural cavity was exposed by incision through the posterior periosteum of the seventh rib. The left lung was found to be adherent to the anterior wall of the chest. These adhesions were separated, and the upper lobe of the lung was found to be adherent to the cystic mass in the anterior and superior mediastinum. The median surface of the upper lobe of the lung was separated from the cystic mass and from the pericardium to which it was also adherent. The adhesions were firm and almost throughout necessitated dissection with the knife. After the lung had been separated from the tumor, the tumor was found to be adherent to the upper portion of the pericardium, to the pulmonary artery and to the ascending aorta, with an irregular projection extending under the arch of the aorta. The tumor also was adherent to the sternum and to the right mediastinal pleura, from which it was separated without opening into the right pleural cavity. The sac was ruptured during its removal, was found to be

multilocular and to contain sebaceous material and hair. The cut ends of the fourth, fifth, sixth and eighth ribs were then tied together and the pleural cavity was completely closed with running sutures of plain catgut. The lung was inflated by positive pressure just before the thoracic cavity was closed. The patient stood the operation satisfactorily. The blood pressure was 95 systolic and 75 diastolic, measured in millimeters of mercury, and the pulse rate was 120.

The operative diagnosis was of intrathoracic teratoma (dermoid) of the anterior and superior mediastinum, projecting slightly more into the left side of the thoracic cavity than into the right side. Pathologic examination disclosed a mediastinal dermoid cyst containing hair, sebaceous material, sweat glands, sebaceous glands and thymic tissue. The cyst probably had originated in the thymus gland (fig 7).



Fig. 5 (case 3)—Anteroposterior view taken at time of patient's admission showing tumor in the upper left mediastinum anteriorly, probably benign.

Convalescence was uneventful except for slight pleural effusion which did not require aspiration. The pulse rate remained at about 120 for three days and then gradually dropped to 90 by the tenth day. The temperature varied between 100 and 99.5 F. until the ninth day, when it dropped to normal and remained there throughout the ensuing period of convalescence. The patient was dismissed from the hospital and was permitted to return home on the twenty-fourth day, at which time the wound was entirely healed.

Roentgenographic examination of the thorax at the time of her dismissal showed the lung to be completely expanded. She returned for observation in about one month at which time she was found to be in excellent general condition. Symptoms were relieved completely (fig. 8).

The clinical history in this case is of interest in that the lesion was, at the onset, diagnosed as an inflammatory condition of the pleura. The

history was that of progressive, increasing pressure in the mediastinum. There was marked dyspnea, and a choking sensation, which probably were the result of pressure on the great vessels of the mediastinum. This pressure, in turn, was caused by gradual increase in the development of the tumor. The pressure became so great as to cause slight bulging at the sternal end of the second rib on the left side. The roentgenograms of the

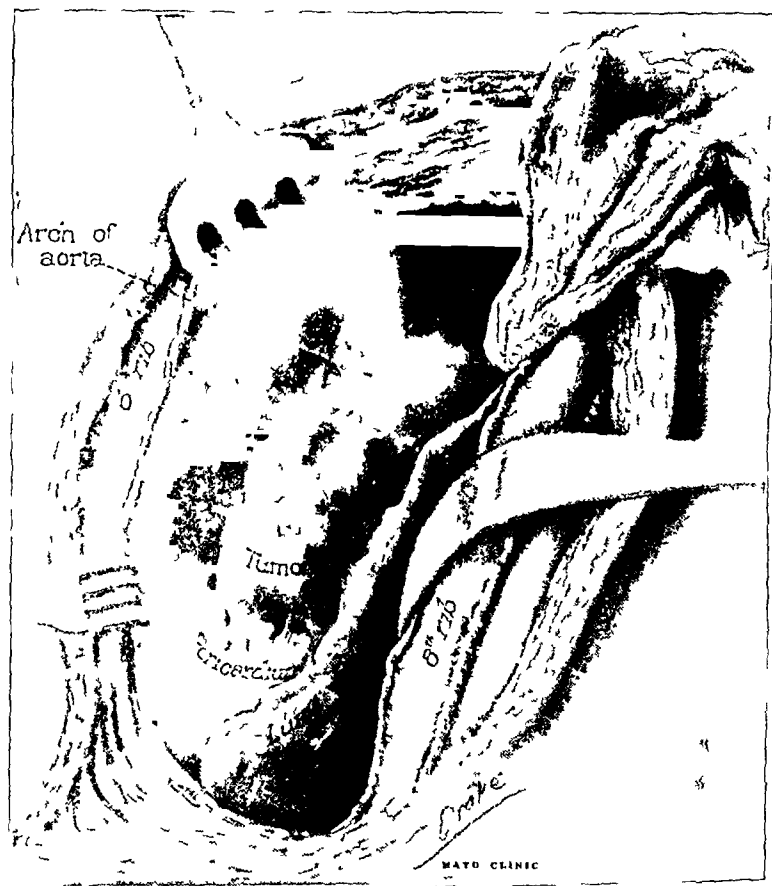


Fig 6 (case 3) —Left posterior thoracotomy with resection of the seventh rib and transpleural exposure of the anterior mediastinal teratoma

thorax were accurate in localizing the tumor and in giving the probable diagnosis in this case. The surgical approach, through posterior thoracotomy, was satisfactory in that the adherent lung was readily separated from the tumor. The lung was allowed partially to collapse. This brought the mediastinal structures clearly into view. The tumor then could be separated from the pericardium and great vessels with little



Fig. 7 (case 3).—Mediastinal teratoma (dermoid cyst) containing hair, sebaceous material, sweat glands, sebaceous glands and thymic tissue. The cyst measured 6 by 5 by 5 cm. and probably originated in the thymus gland.

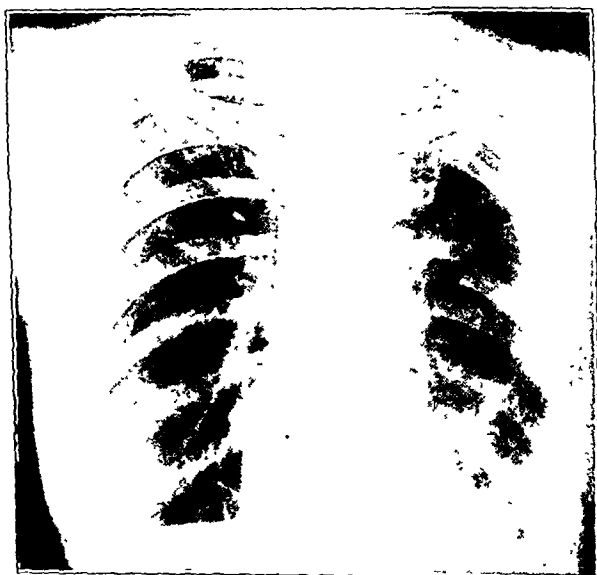


Fig. 8 (case 3).—Pleuritic adhesions of the left base and lung fully reexpanded six weeks after transpleural complete removal of the anterior mediastinal teratoma, resection of the seventh rib, and section of the eighth, fifth and fourth ribs.

danger of injury. The mediastinal pleura of the right pleural cavity could be separated easily from the wall of the tumor with the minimal danger of injury or of pneumothorax on the right side.

CASE 4.—A woman, aged 19, was admitted to the clinic on Oct. 18, 1928. The final diagnosis was intrapulmonary teratoma (congenital cyst) of the middle and lower lobes of the right lung. The chief complaint was pain in the right side of the chest of one year's duration. She had been in good health until one year before admission, when she had begun to have severe sharp pains in the right side of the chest, anteriorly and extending along the right costal margin posteriorly. The pain had been like that of pleurisy and had been noted especially on deep breathing, coughing, sneezing and so forth. The pain had been so troublesome that she had consulted her home physician one year before she had come to the clinic, but nothing had been found. The pain had been intermittent and had disappeared entirely for from two to three weeks at a time, until one month before admission, when she had become acutely ill and had been in bed for one week with severe pain in the anterior right portion of the chest. There had been marked dyspnea and moderate fever. A diagnosis of pneumonia had been made at that time. She had not had cough or night sweats and had not lost weight until shortly before she had come to the clinic. Dyspnea on slight exertion had been present for a year. Flecks of blood had been noted in the sputum for one month.

The results of general examination were essentially negative, except for the discovery of a localized area of dullness in the right anterior part of the chest, with absence of breath sounds in this area. There was evidence of slight loss of weight. There was moderate secondary anemia, with hemoglobin of 58 per cent. The Wassermann reaction of the blood was negative. Examination of sputum was negative for bacilli of tuberculosis. Roentgenograms of the thorax revealed a large, infiltrating tumor extending from the seventh to the tenth ribs posteriorly, which apparently arose in the hilum of the right lung. The lateral view revealed a large tumor in the right anterior portion of the thorax (fig. 9 A and B).

As part of the preoperative preparation, bronchoscopy was done Oct. 24, 1928. Results were indeterminate. There was no evidence of an intrapulmonary tumor but slight compression of the right main bronchus suggested the presence of an extrapulmonary tumor causing pressure on the bronchus.

Right posterior thoracotomy was done Oct. 31, 1928, with removal of the seventh rib. Transpleural complete removal of the intrathoracic tumor was effected. Transfusion of 500 cc. of blood was carried out. The pleural cavity was drained by intercostal closed drainage through the ninth intercostal space. Intratracheal ethylene and ether anesthesia were employed. Approach was through an incision made parallel with the seventh rib, from the posterior angle to the sternum. The seventh rib was removed by subperiosteal resection, and the pleural cavity was opened by incision through the posterior periosteum. On exploration of the right thoracic cavity, the diaphragm was found to be firmly adherent to the lower lobe of the right lung posteriorly. The adhesions were separated. The anterior portion of all three lobes of the lung was adherent to the lateral anterior wall of the chest and to the diaphragm. The adhesions were partially separated from the middle and upper lobes, allowing them to retract backward. It was possible to feel a large cystic tumor, completely surrounded by pulmonary tissue which was collapsed over the surface of the tumor. The tumor seemed to be in the center of the lung, with a small projection into the posterior mediastinum. As it was situated in the fissure between the upper and lower lobes, posteriorly, it was firmly adherent to all three lobes as well as to a

portion of the pericardial sac. The adhesions were separated, and a portion of the tumor was found close to the hilum, completely surrounded by pulmonary tissue of the upper lobe. This pulmonary tissue had to be cut through in order to uncover the upper portion of the wall of the cyst. The cyst was inflammatory and was so adherent to the surrounding pulmonary tissue that it had to be dissected free with a knife. It ruptured during removal and was found to contain about 250 cc. of dark, brownish-green fluid. After the capsule had been dissected away from the surrounding tissues of the middle and upper lobes, the pulmonary tissue was resutured with catgut. The opening in the pleura was completely closed with plain catgut and the muscles of the thoracic wall were resutured. The incision in the skin was then completely closed (fig. 10).

The operative diagnosis was of a large intrathoracic cystic teratoma, 10 by 15 cm., originating close to the hilum of the right lung, extending partly into the

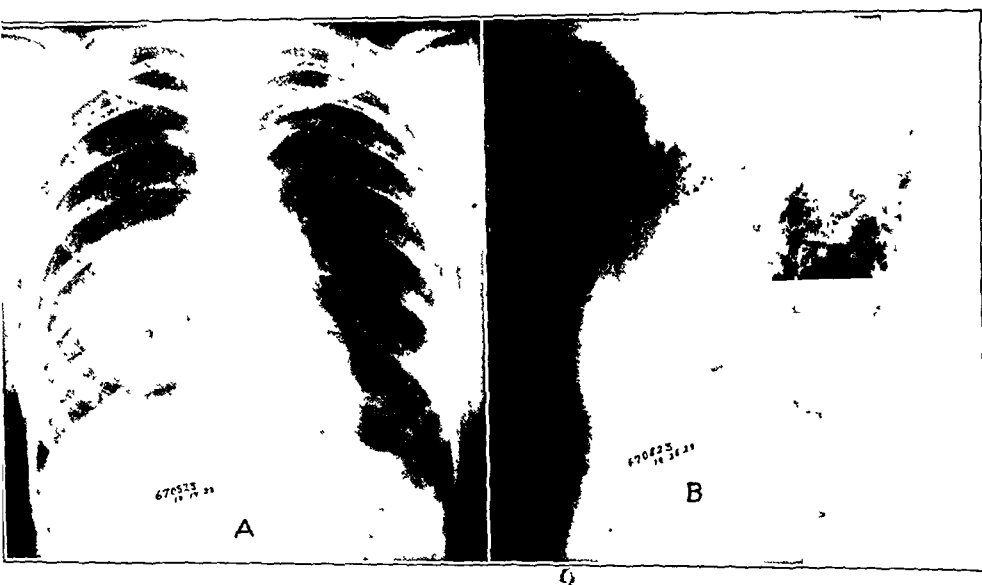


Fig. 9 (case 4).—*A*, anteroposterior view at time of patient's admission showing large infiltrating tumor extending from the seventh to the tenth ribs posteriorly, apparently arising in the hilum of the right lung; *B*, lateral view at time of admission showing large tumor of anterior portion of the right side of the thorax.

fissure between the upper and lower lobes of the lung posteriorly, and completely surrounded by pulmonary tissue, to which it was adherent.

Pathologic study disclosed a cystic mass composed of a cyst with a fibrous wall which was filled with clotted blood. There was no definite epithelial lining. A solid area at one end of the tumor was composed of salivary glands, and of ducts and fibrous tubes, both lined with columnar epithelium that closely resembled epithelium of the bronchi.

The immediate reaction to the operation was satisfactory. The pulse was 140 and the temperature 103 F. on the first day. The temperature dropped to normal on the fourth day and the pulse rate gradually dropped to 86. The intercostal drainage tube was used as a channel for irrigation with a surgical solution of

chlorinated soda, and in this way bloody fluid was removed from the pleural cavity. After the eighth day, fluid could not be recovered, and the tube was removed on the tenth day. Two days later the temperature gradually began to rise. On the seventeenth day the pleural cavity again was aspirated and fluid was found. Following the removal of the fluid the temperature dropped to normal and remained normal until the twenty-eighth day; then it suddenly rose to 101 F. A slight cold developed; the patient ran a septic temperature, which rose to 102 F. On the twenty-ninth day, therefore, a portion of the ninth rib was resected, and



Fig. 10 (case 4).—Transpleural exposure of large right posterior mediastinal teratoma adherent to the diaphragm and to the middle and lower lobes of the right lung which were partially collapsed and adherent over its surface.

a tube was inserted in the chest. A small empyema cavity was found. The temperature dropped to normal on the eighth day following the insertion of the tube. The tube gradually was removed, and the empyema cavity was entirely obliterated in three weeks following this operation. The patient was dismissed two months after the removal of the intrathoracic tumor. The lung was completely expanded and the patient was relieved from symptoms (fig. 11).

The clinical history in this case closely simulated that of the preceding case in that at the onset the condition was thought to be an inflammatory pleural or pulmonary lesion. The presence of moderate fever during the attacks of illness would indicate an inflammatory reaction in the tumor itself, which probably caused gradual increase in the size of the tumor which, in turn, produced progressive symptoms of pressure within the mediastinum and thorax. In this instance, the tumor was of sufficient size to cause partial collapse of the lung. The bronchoscopic examination was of aid in ruling out intrapulmonary lesions, and the slight compression of the right main bronchus suggested an extrinsic



Fig. 11 (case 4).—Slight elevation of diaphragm. Normal appearance of lungs two months after transpleural complete removal of mediastinal teratoma and resection of seventh rib and portion of ninth rib.

tumor. The value of latent roentgenograms was exemplified in this case. The anteroposterior stereoscopic views showed evidence of an infiltrating type of tumor, suggesting that a malignant condition was present. This hazy outline probably was the result of the lung being collapsed around the surface of the tumor. The lateral views disclosed that the posterior surface of the tumor had a smooth round appearance which strongly suggested the presence of a benign lesion. The surgical approach by posterior thoracotomy was satisfactory and the marked inflammatory reaction in the tumor was evidenced by the firm adhesions

to the lower lobe of the lung which made it necessary to cut through the pulmonary tissue in order to remove the capsule of the tumor. Because of the marked inflammatory reaction of all of the surrounding structures and the numerous bleeding points in the bed of the tumor, it was thought best to institute intercostal closed drainage in this case at the time of the operation. This complication prolonged convalescence from three to four weeks before the empyema wound was entirely healed.

CASE 5.—A man, aged 49, was admitted to the clinic on Feb. 12, 1929. The final diagnosis was large anterior and superior mediastinal multilocular cystic squamous cell epithelioma, graded 4, probably malignant degeneration of a teratoma. The chief complaint was pain in the left part of the chest and the left arm, of four years' duration. The patient first had noticed pain in the left upper anterior part of the chest and the left arm four years before admission. This had come on by spells and had been more or less severe. The patient had been fairly well until about three months before he came to the clinic, when the pain had become more or less constant and severe and sedatives had been required. For nine months he had noticed that it was hard for him to lie down, particularly on the left side, because of the pain and drawing sensation in the anterior upper portion of the chest. He had felt much better when he was up and about and he had not coughed or expectorated. He had had occasional night sweats and sharp pain in the left shoulder. The appetite had been fair, but he had gradually lost strength. He had lost 24 pounds (10.9 Kg.) during the last seven months.

General examination revealed moderate emaciation and moderate arteriosclerosis. There was dullness to percussion, and bronchial breathing in the upper left part of the chest both anteriorly and posteriorly. Moderate clubbing of fingers also was noted. Urinalysis gave negative results. The hemoglobin was 78 per cent and the leukocytes numbered 6,800 per cubic millimeter. The Wassermann reaction of the blood was negative. Roentgenograms of the thorax revealed evidence of a rounded, somewhat lobulated tumor in the left part of the mediastinum. The lateral view showed the tumor to be in the middle portion of the mediastinum. Fluoroscopic examination showed that the tumor was pulsile, possibly an aneurysm (figs. 12 A and B).

Preoperative preparation included left pneumothorax that was done for diagnosis. Roentgenograms taken after pneumothorax revealed evidence that there was a large lobulated tumor in the right lung, situated about midway anteroposteriorly, and that the lung was collapsed over the tumor. Fluoroscopic examination showed the tumor to be nonexpansile.

Posterior left thoracotomy was done on Feb. 20, 1929, with resection of 16 cm. of the eighth rib and section of the ninth, seventh, sixth and fifth ribs. Transpleural complete removal of the intrathoracic tumor was effected. Transfusion of 500 cc. of blood was carried out. The thoracic cavity was closed without drainage. Intratracheal ethylene anesthesia was used. The left pleural cavity was opened by incising the pleura through the periosteum of the eighth rib. On exposing the anterior mediastinum, a multilocular, lobular, hard cystic mass could be felt between the lung and the pericardium and great vessels. The greater portion of the tumor extended into the left side of the thorax. The entire median portion of the lung between the upper and lower lobes was firmly adherent over the surface of the tumor, and the upper lobe was about a third collapsed by the tumor. The lung also was firmly adherent to the parietal pleura at the apex. The adhesions were old and vascular and had to be cut and ligated.

After the lung was dissected from the parietal pleura at the apex, the median portion was dissected from the tumor. The adhesions were so firm that sharp dissection with a knife was necessary. In some areas, it was necessary to remove the visceral pleura because of the firm adhesions. After the lung had been dissected free, the mass was found to be adherent to the upper third of the pericardium and to the great vessels in the mediastinum. Dissection was then started from the pericardium. The wall of the cyst was ruptured in an attempt to remove it and about 700 cc. of dark brownish fluid and granular material escaped. The sac was multilocular and lobulated and was firmly adherent to the pericardium, pulmonary artery, ascending aorta and the arch of the aorta, as well as to the right mediastinal pleura. It was impossible to follow any line of



Fig 12 (case 5).—*A*, anteroposterior view on patient's admission, following artificial pneumothorax showing large rounded tumor of the left lung, pneumothorax, and collapse of the lung around the tumor; *B*, lateral view following artificial pneumothorax showing large lobulated tumor about midway anteroposteriorly, apparently arising from the anterior mediastinum. The posterior mediastinum is clear.

cleavage and the entire capsule had to be dissected away from these structures. A small portion of the outer wall of the sac was left adherent to the pulmonary artery and another small portion, which had projected under the arch of the aorta, was left in place. After the tumor had been removed, all bleeding points were controlled by ligatures. The cut ribs were sutured together with chromic catgut and the thoracic cavity was closed without drainage. The patient's condition at the close of the operation was fair. The blood pressure was 95 systolic and 75 diastolic, and the pulse rate was 116 (fig. 13).

The operative diagnosis was large anterior and superior mediastinal multilocular cystic squamous cell epithelioma, graded 4, probably malignant degeneration of a teratoma. The tumor was 20 by 18 by 15 cm. and was situated in the anterior and superior mediastinum, extending slightly into the right pleural cavity, and was adherent to the right pleura. There was a large projection into the left pleural cavity, with partial collapse of the left lung. Pathologic examination disclosed a degenerated, infected, squamous-cell epithelioma, graded 4 (fig. 14).

The patient's immediate reaction was satisfactory. The pulse rate varied from 110 to 130 for the first five days. The temperature was 101.5 F. on the second day and dropped to normal on the third day, with remissions to 100; it varied between 100 and normal until the sixth day. The respiratory rate ranged between 24 and



Fig. 13 (case 5).—Site of the large multilocular cystic anterior mediastinal tumor firmly adherent to the pericardium, arch of the aorta, pulmonary artery and median surface of the left lung.

32 until the seventh day. Bloody fluid was aspirated daily from the chest after the third day. The patient's condition seemed to be progressing satisfactorily until the evening of the sixth day, when he had a sudden rise of temperature to 105 F. with increase in pulse rate from 110 to 150 and in respiratory rate to 44. He became irrational, partial paralysis of the left side developed and he died on the morning of the seventh day from cerebral embolism.

The duration of symptoms, in this case, over a period of four years, would suggest the presence of a benign tumor which had undergone malignant degeneration. It is the largest tumor which I have encoun-

tered situated in the anterior mediastinum. Its situation was like that of the tumors in the two preceding cases; however, this tumor was much larger and even more adherent to the surrounding structures. The capsule of the cyst was under marked tension from the contained fluid, and it was ruptured during its removal. The greater portion of the wall had to be dissected in pieces away from the surrounding structures and was found, on microscopic examination, to consist almost entirely of fibrous tissue except a portion of it which was situated in the anterior mediastinum above the arch of the aorta. It was in this portion of the capsule of the tumor that squamous cell epithelioma was found. The



Fig. 14 (case 5).—Squamous cell epithelioma, graded 4 (probably a malignant degeneration of a teratoma).

definitely encapsulated nature of the tumor and the fact that it had not infiltrated into the surrounding structures, indicate that originally it was probably a benign tumor. This emphasizes the importance of early diagnosis and of early surgical intervention in all cases of intrathoracic tumor except those in which a hopeless prognosis is obvious. This case was the only one in the whole series in which there was an operative death. The weakened condition of the patient and his loss of weight during the last three months were unquestionably factors in his inability to survive the operation. The partial collapse of the lung had produced slight bronchiectasis in the lower lobe, and this may have been a factor in the production of the cerebral embolism. Examination at necropsy

showed that the tumor had been removed completely and that the operative field was in good condition. There was no remaining evidence of malignancy in the surrounding structures.

CASE 6.—A married woman, aged 35, was admitted to the clinic on Feb. 14, 1928. The final diagnosis was intrathoracic neurofibroma of the right part of the wall of the chest. The chief complaint was fatigue of two years' duration. There was soreness in the right shoulder and tumor of the right wall of the chest of eight years' duration.

The patient came to the clinic with multiple complaints of the type heard in cases of chronic nervous exhaustion, with marked anemia of indeterminate type. The hemoglobin was 36 per cent. This probably was responsible for a great many of the patient's general symptoms. She had a small tumor of the right lower portion of the thoracic wall, between the eighth and ninth ribs, in the midaxillary line. She complained of periodic pain at the site of this tumor. The growth was slightly movable, and seemed to come through the wall of the chest. She had noticed the presence of the tumor about eight years before admission, and there had been gradual increase in size. She was placed in the hospital under study for the anemia and was given two transfusions of blood, with only slight improvement in the condition. Removal of the intrathoracic tumor was advised.

General examination revealed a tumor at the eighth intercostal space, in the midaxillary line, on the right side. The tumor was freely movable. The hemoglobin was 36 per cent; erythrocytes numbered 3,650,000 and leukocytes 8,000 per cubic millimeter. Roentgenograms of the thorax showed evidence of a circumscribed tumor arising from the parietal pleura, in the lateral aspect of the lower right part of the chest, and it probably was benign (fig. 15A).

Preoperative preparation included transfusion of 500 cc. of blood, March 2, 1928. This was given because of the marked anemia of indeterminate, although probably secondary, type.

Posterior right thoracotomy, with partial removal of the seventh, eighth, ninth and tenth ribs, was done March 7. Transpleural complete removal of the intrathoracic neurofibroma was effected. The thoracic cavity was closed without drainage. Intratracheal ether and ethylene anesthesia was used. Incision was made over the eighth rib, on the right posterolateral portion of the wall of the chest, and a small protruding part of the tumor was found between the eighth and ninth ribs. The large mass of the tumor was protruding into the thoracic cavity and extended from the seventh to the tenth ribs. The ribs were resected well beyond the limits of the tumor and were removed, in one mass, with that portion of the wall of the chest and pleura which was adherent to the tumor. The latissimus dorsi and serratus muscles were stitched over the area of the wall of the chest and the wound was closed without drainage.

The operative diagnosis was intrathoracic degenerating neurofibroma of the right side of the chest, situated in the posterior axillary line and protruding between the eighth and ninth ribs. Pathologic examination revealed a cystic, hemorrhagic, degenerating neurofibroma. Convalescence was uneventful except for pleural effusion on the right side which necessitated aspiration on two occasions. The patient was dismissed from the hospital and from my care on the twenty-fourth day, with the wound entirely healed. At the time of her last visit, one year following the operation, she had no respiratory symptoms and had gained about 23 pounds (10.4 Kg.). The roentgenograms of the thorax showed the lungs to be normal. The hemoglobin had increased to 59 per cent and the erythro-

cytes to 4,380,000 per cubic millimeter. The leukocytes numbered 7,600 per cubic millimeter (fig. 15 *B*).

The secondary anemia which was present in this case was not the result of the tumor but was an associated condition. Operation was advised because of the presence of the tumor in the thorax which was undoubtedly the cause of the pain in the right lower part of the thorax. This tumor was under so much tension under the pleura that it had bulged through the eighth intercostal space. Since the opening in the pleural cavity was closed with muscle of the wall of the chest, accumulation of serum resulted which necessitated aspiration. Marked improvement in the patient's general condition followed the operation. Not only

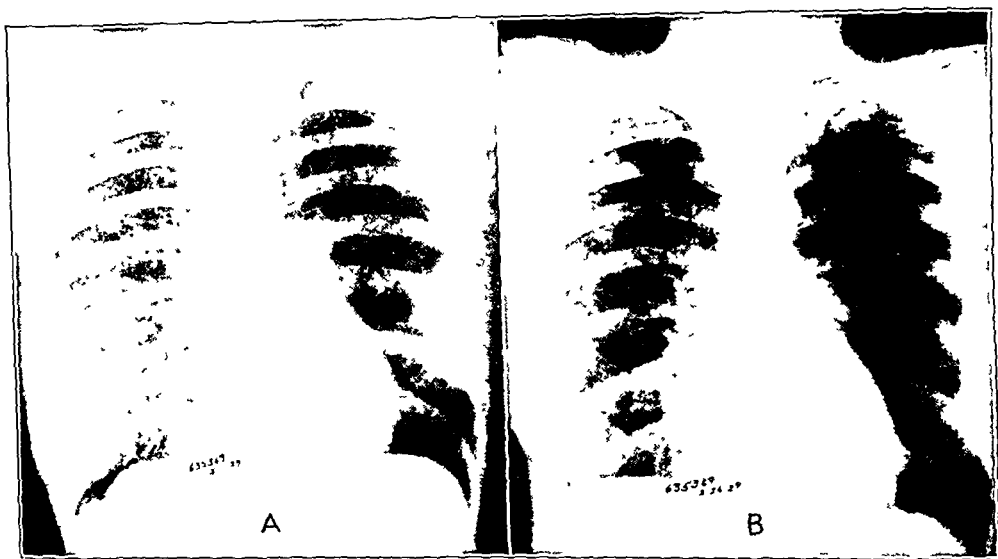


Fig. 15 (case 6).—*A*, circumscribed tumor in the lower portion of the right side of the chest presenting between the eighth and ninth ribs in the posterior axillary line and extending into the thorax from the seventh to the tenth ribs at time of patient's admission; *B*, roentgenogram taken one year after transpleural removal of large intrathoracic neurofibroma and partial resection of seventh, eighth, ninth and tenth ribs. The lung is fully reexpanded.

did she have entire relief from pain in the right lower portion of the thorax, but the anemia also showed marked improvement, which probably resulted from the improved general condition.

CASE 7.—A married woman, aged 46, was admitted to the clinic on Sept. 15, 1926. The final diagnosis was of large intrathoracic neurofibroma in the right upper part of the posterior mediastinum. The chief complaint was palpitation, and dyspnea on exertion, of two years' duration.

Two years before admission the patient had noted loss of initiative and of energy and was easily fatigued. Palpitation of the heart, shortness of breath on

exertion and tremor with marked nervousness gradually had developed. The symptoms had become more severe during the six months previous to admission. For one month she had noticed edema of the feet. She had lost 15 pounds (6.8 Kg.). She had gone to a hospital six weeks previous to her visit to the clinic and had been given treatment with iodine for three weeks, during which time she had regained 5 pounds (2.3 Kg.). She had had some difficulty in swallowing toast or crackers, which seemed to stick in her throat.

Results of general examination were essentially negative except for signs of the presence of a solid tumor in the upper posterior right portion of the thorax. The hemoglobin was 72 per cent, erythrocytes numbered 4,350,000 and leukocytes 5,800 per cubic millimeter. The Wassermann reaction of the blood was negative. The basal metabolic rate was -8. Roentgenograms of the thorax gave evidence of a large, circumscribed tumor in the upper part of the right lung. Fluoroscopic



Fig. 16 (case 7).—Large circumscribed tumor in the upper portion of the right side of the thorax extending from the third to the eighth rib posteriorly at time of patient's admission.

examination indicated that there was a nonpulsating tumor in the upper right part of the chest and that probably it was benign (fig. 16).

High right posterior thoracotomy was done Sept. 25, 1926, with removal of a portion of the seventh rib and section of the fourth, fifth, sixth and eighth ribs. Extrapleural complete removal of intrathoracic tumor was effected. The thoracic cavity was closed without drainage. Intratracheal ether anesthesia was used. A posterolateral incision was made between the scapula and the spinal column, along the seventh rib, and about 12 to 14 cm. of the rib was removed subperiosteally. The posterior periosteum then was incised and the pleura was separated from the thoracic wall. The sixth, fifth, fourth and eighth ribs then were divided, and the pleura was separated from the wall of the thorax, from the posterior to anterior

aspect, without opening into the thoracic cavity at any point. The tumor was adherent to the thoracic wall, close to the spinal column, at the level of the fifth rib. The pleura was adherent to the tumor; the anterior portion could not be entirely separated from the tumor and was removed with it. The opening in the pleura was sutured with plain catgut. The ribs were drilled and sutured together with chromic catgut and the wound was completely closed (fig. 17).

The operative diagnosis was of large, intrathoracic neurofibroma of the upper right portion of the posterior mediastinum. Pathologic examination disclosed a neurofibroma, weighing 234 Gm.

Moderate shock immediately followed operation. On the third day, the temperature was 102 F., the pulse was 130 and respirations, from 34 to 40. These values remained fairly stationary until the fifth day, when gradual improvement began. On the eighth day, the temperature reached normal, the pulse rate was 90 and respirations, 28. Physical signs and roentgenographic examination showed

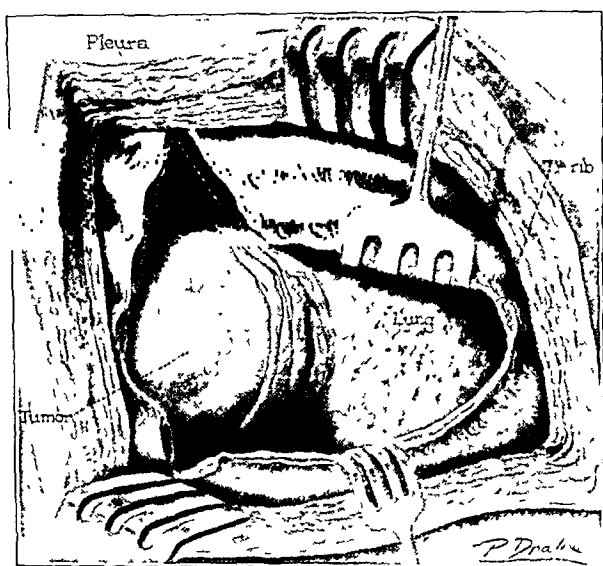


Fig. 17 (case 7).—Intrathoracic neurofibroma of the posterior mediastinum. Extrapleural exposure of the tumor.

evidence of fluid in the pleural cavity, necessitating aspiration on one occasion. The patient's temperature was normal from the nineteenth day, the pulse remained between 70 and 76, and respirations between 20 and 24. She was dismissed from my care one month following operation; the wound was entirely healed and she was feeling well generally. Roentgenographic examination did not afford evidence of fluid in the pleural cavity. Roentgenograms of the thorax two years after operation showed the lungs to be free from disease, and the general condition of the patient was excellent. There was no evidence of return of the tumor (figs. 18 and 19).

This case is of interest because of the various symptoms which were associated with a tumor of this size situated in the posterior mediastinum. Because of the patient's multiple complaints, it was difficult to evaluate

how many of the symptoms were the result of the tumor. Tumors situated in the middle portion of the thorax posteriorly rarely give symptoms until they are of sufficient size to cause marked collapse of the lung. The benign tumors in this area probably are the most silent tumors of the thorax. This is the only case in this group in which it was possible to remove the tumor by extrapleural operation. In this instance, a small area of the pleura was opened because of adhesions to the tumor. As was noted, pleural effusion occurred postoperatively, necessitating one aspiration. It has been my experience that the pleura has been adherent to the tumors in all cases in which I have operated.

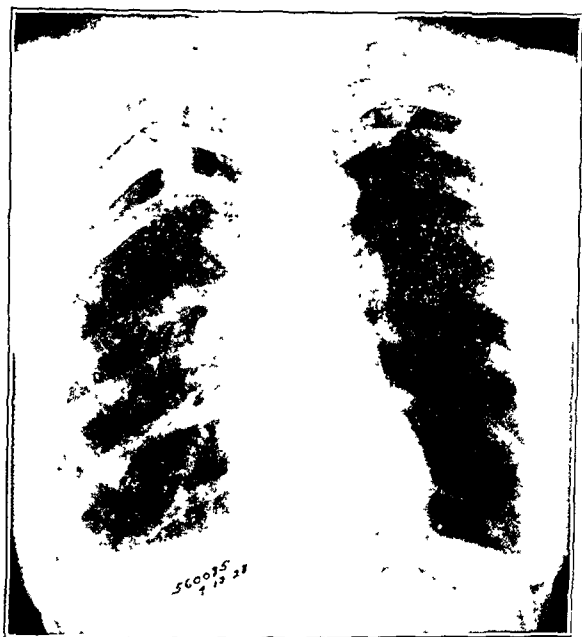


Fig. 18 (case 7).—Roentgenogram taken two years after extrapleural removal of large intrathoracic neurofibroma. Old fracture of the fourth, fifth, sixth and eighth ribs is shown with firm union with absence of the seventh rib posteriorly. Appearance of the lungs is normal.

I do not believe it advisable to attempt extrapleural removal because marked separation of the pleura from the thoracic wall is necessary and usually the pleural cavity ultimately has to be opened.

CASE 8.—A married woman, aged 35, was admitted to the clinic on March 19, 1928. The final diagnosis was large left intrathoracic cellular fibroma. The chief complaint was pain in the upper left part of the chest of about nine years' duration. The onset of the complaint began nine years before admission, while the patient was working on a farm, stacking hay and carrying heavy weights. She first had noticed pain in the upper left part of the thorax. It had been periodic

for six years, and usually had been noted following extreme exertion. The pain had become severe, with marked dyspnea, and the patient had been confined to bed. At this time a diagnosis of tuberculosis had been made. Four liters of clear fluid had been removed by aspiration from the left pleural cavity. For the next two years the pain had been more or less constant, and more severe on exertion. A year and a half before she came to the clinic, about 2 liters of clear fluid were removed by aspiration from the left side of the thorax. For the year before admission, the pain gradually had extended from the left upper portion of the thorax to the left axilla, left shoulder and left side of the neck. This pain had become progressively worse but could be relieved by hot applications. The

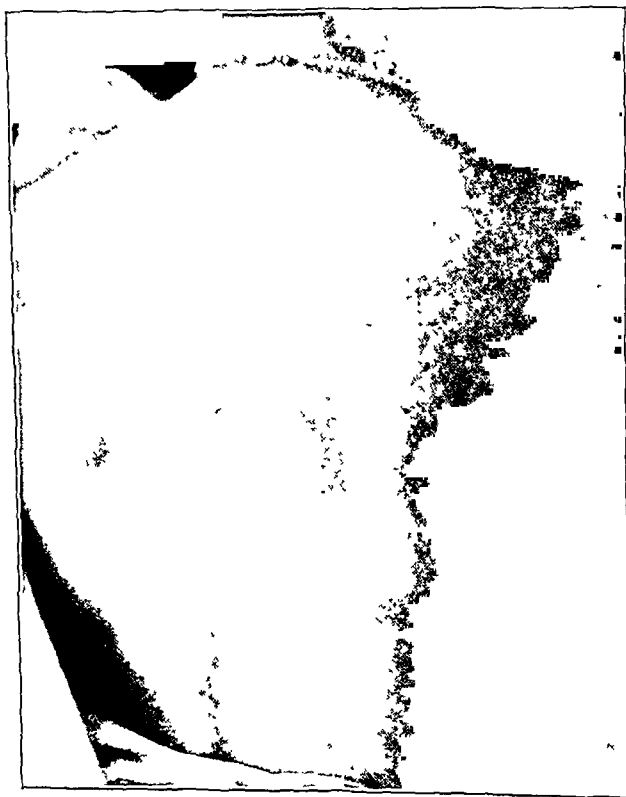


Fig 19 (case 7).—Two years after extrapleural removal of large right intrathoracic neurofibroma.

dyspnea had become progressively more marked. She had not had cough, expectoration or loss of weight.

Results of general examination were essentially negative except for dullness on percussion and absence of breath sounds in the greater portion of the left lung, with dullness extending beyond the sternum, to the right side of the chest. Urinalysis gave negative results. The hemoglobin was 72 per cent and the Wassermann reaction of the blood was negative. The sputum was negative for bacilli of tuberculosis. Roentgenograms of the thorax revealed evidence of a large intrathoracic tumor involving the upper two thirds of the left side of the thorax, probably primarily benign but now malignant (fig. 20).

Left posterior thoracotomy, with removal of a portion of the seventh rib and section of the fourth, fifth, sixth and eighth ribs, was done April 21, 1928. Trans-pleural complete removal of the intrathoracic tumor was accomplished. The thoracic cavity was closed without drainage. Intratracheal ether and ethylene anesthesia was used.

On exposing the left pleural cavity, a huge semicystic tumor was found which completely filled the upper two thirds of the thoracic cavity, from the apex to the eighth rib, and pushed the mediastinum to the right. The entire upper lobe of the left lung was collapsed, with partial collapse of the lower lobe. The wall of the tumor was firmly adherent to the pleura, and there was a firm attachment posteriorly, along the line of the spinal column. Most of the tumor was solid, but there were several lobulated cystic areas, a great many of which were ruptured



Fig. 20 (case 8).—Large intrathoracic tumor completely filling the entire left upper portion of the thorax to level of the ninth rib posteriorly at time of patient's admission. The trachea is markedly displaced to the right.

during removal and were found to contain about 1,200 cc. of blood-tinged serous fluid. The rupture of these cystic regions reduced the size of the tumor at least half. The entire tumor was removed and the thoracic cavity was closed (figs. 21, 22, 23 and 24).

The operative diagnosis was of a large intrathoracic fibroma completely filling the upper two thirds of the left side of the thorax, extending into the posterior mediastinum and pushing the trachea to the right. There was almost complete compression of the left lung. The mediastinum was pushed to the right, with partial compression of the right lung. Pathologic examination revealed a cellular fibroma, weighing 340 Gm. (fig. 25).

There was considerable shock at the time of operation, with a pulse rate of 140 and a temperature of 102 F. in the afternoon of the first day. The patient was given solution of sodium chloride intravenously immediately after the operation and her reaction was satisfactory. The pulse rate dropped to 110 on the second day. On the fourth day, the temperature was normal and the pulse rate, 94.

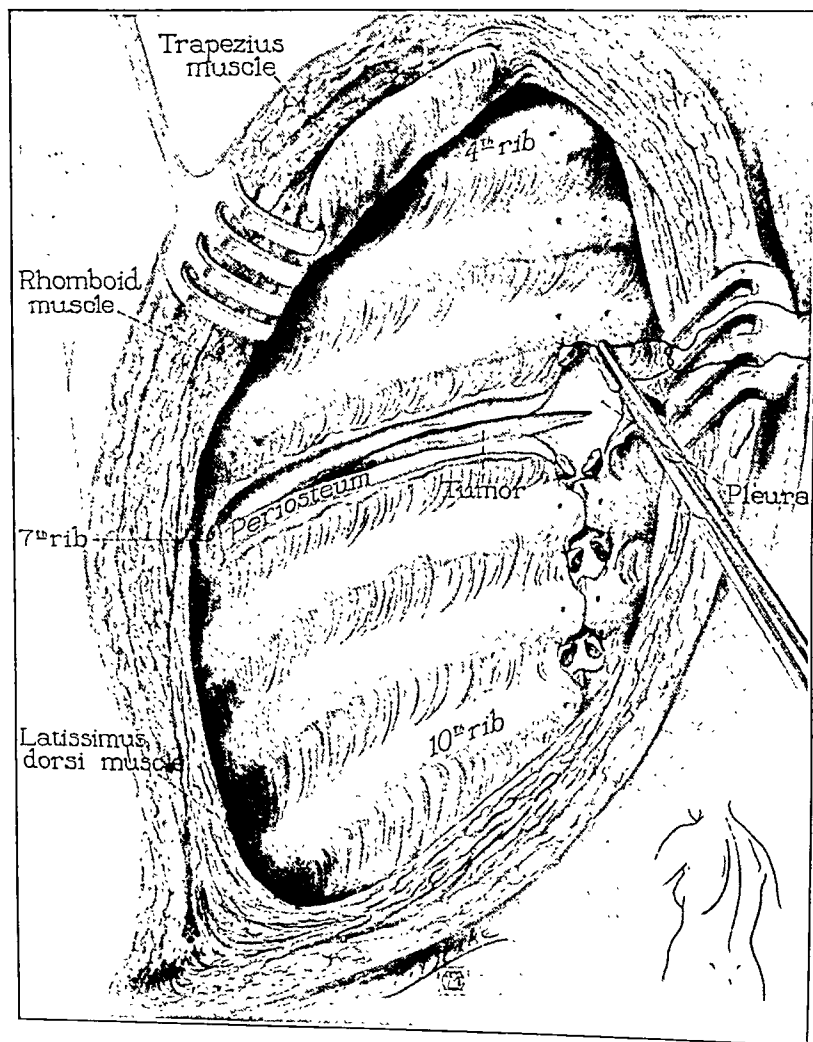


Fig. 21 (case 8).—Insert shows posterolateral incision. Retraction of the scapula forward; resection of the posterior two thirds of the seventh rib. The adjacent ribs were drilled before section; intercostal vessels caught and ligated before section; pleura incised through the posterior periosteum of the resected rib.

Roentgenographic examination of the left pleural cavity revealed fluid which was aspirated on the sixth, eighth and tenth days. Cultures were made of the fluid; growth did not result. On the fourteenth day, fluid again was aspirated from the pleural cavity; 200 cc. was obtained which showed the presence of an

occasional gram-positive coccus. There was gradual expansion of the lung. The patient ran a slight temperature for about a week, and the pleural cavity again was aspirated, with results similar to those obtained previously. On the twenty-eighth day, the temperature dropped to normal and remained practically normal during the remainder of convalescence. The patient was dismissed on the forty-second

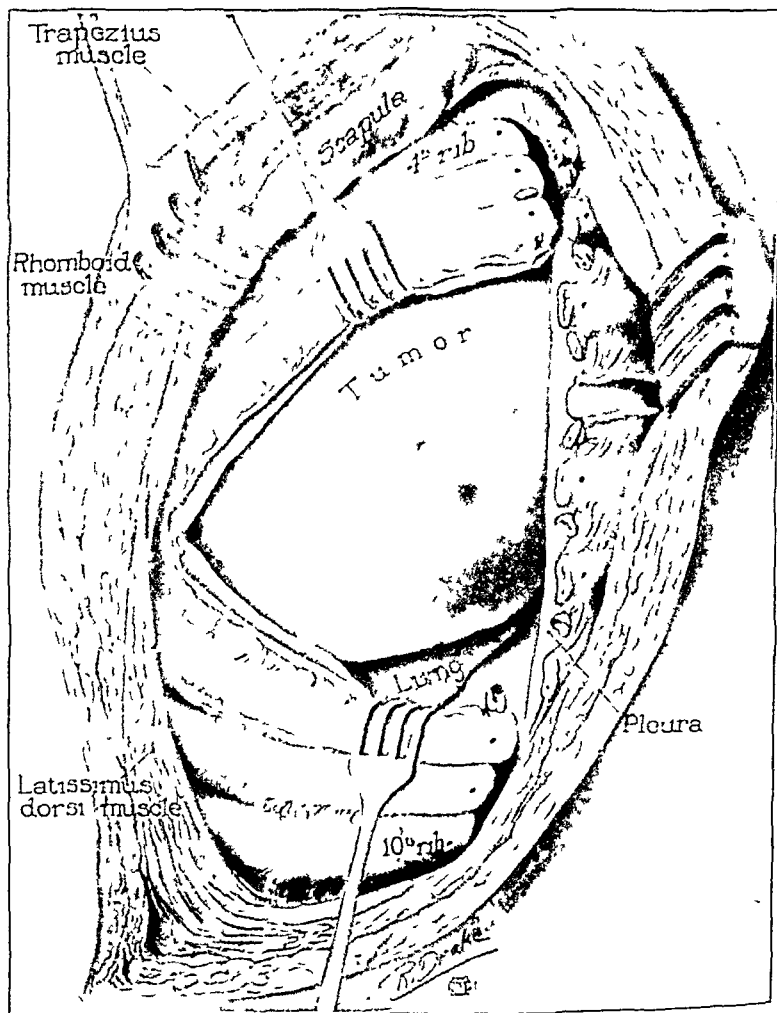


Fig. 22 (case 8).—Section of the fourth, fifth, sixth, eighth and ninth ribs and intercostal muscles. Retraction of the ribs exposing the left pleural cavity. Lower portion of the tumor presenting in the wound. Small portion of collapsed lung can be seen at the lower angle.

day after operation, with the lung completely expanded and with complete relief from symptoms (fig. 26).

The patient returned for observation about six months following the removal of the intrathoracic tumor. Her general condition had markedly improved and

she had gained 15 pounds (68 Kg.). She had practically no dyspnea on exertion. Roentgenographic examination showed that the left lung was completely expanded (fig. 27).

The clinical history, in this case, extending over a period of nine years, and the fact that the patient remained in good general condition

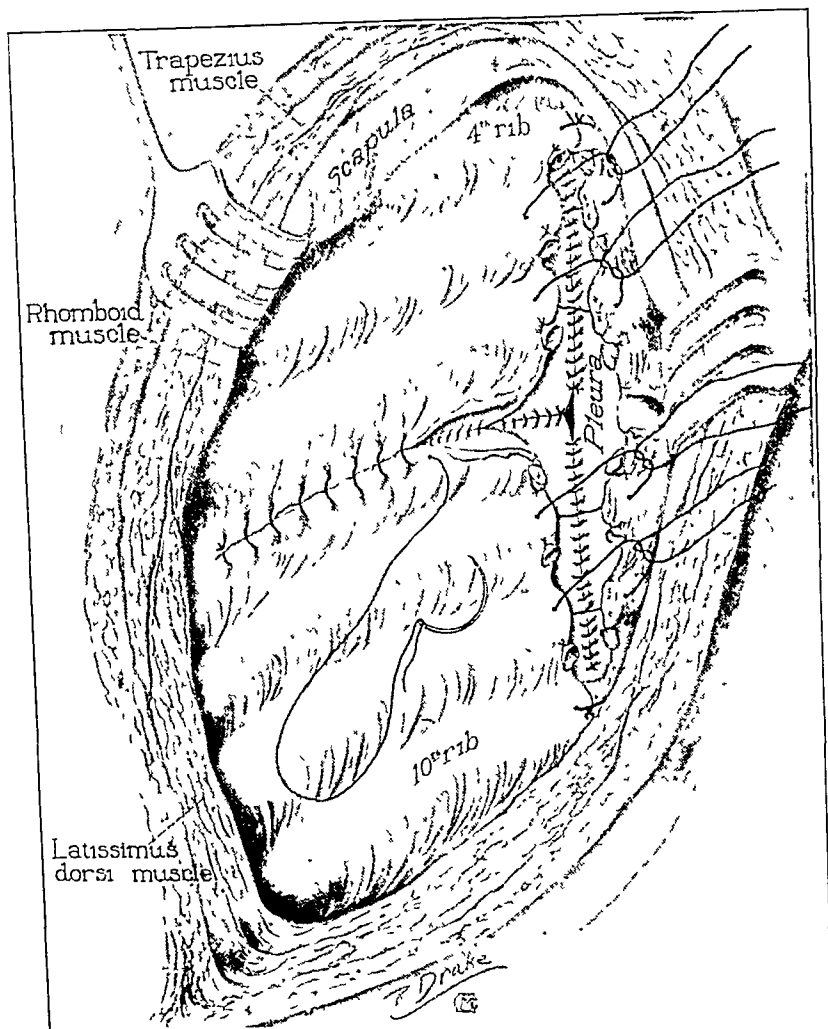


Fig. 23 (case 8).—Pleura closed with continuous catgut sutures; cut ends of ribs tied with chromic catgut.

suggested that a benign lesion was present. The progressive symptoms were caused by increasing pressure on the mediastinal structures and collapse of the lung, due to the growth of the tumor. The early diagnosis of tuberculosis had been made because of the removal, by aspiration, of clear fluid from the thorax. This fluid probably was removed

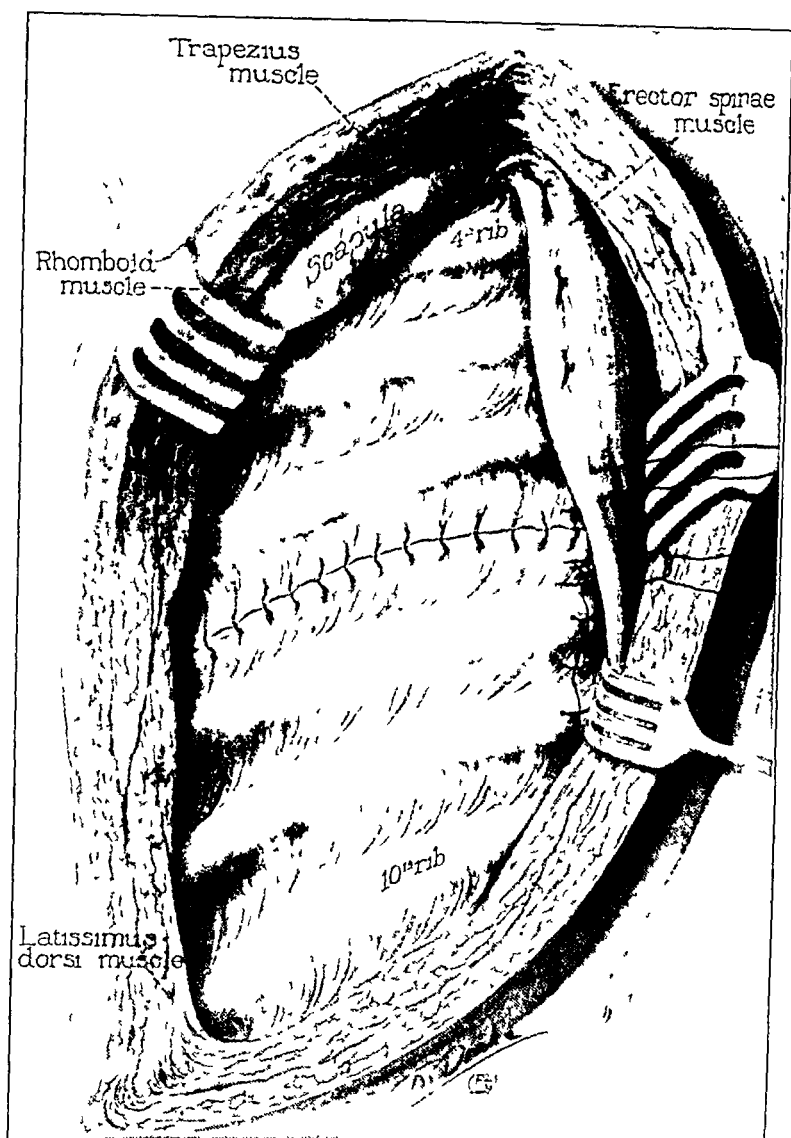


Fig 24 (case 8) —Rectospinous muscles sutured over the vertical incision making the wound airtight after full reexpansion of the lung

from the cystic tumor and not from the pleural cavity. The wall of the tumor was covered with pleura; probably the tumor originated from an intravertebral disk in the upper part of the posterior mediastinum. The operative removal was difficult because of the size of the tumor and because of adhesions of the tumor to the surrounding structures. The posterior operative approach was satisfactory, as it usually is in these large tumors, for the opening in the wall of the chest can be enlarged

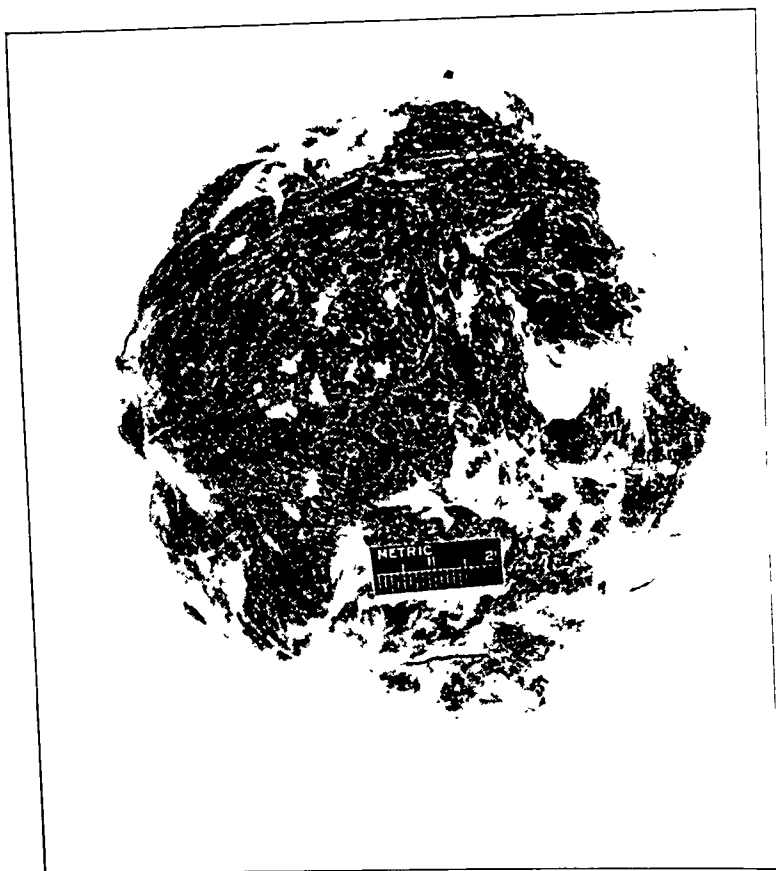


Fig. 25 (case 8).—Large left intrathoracic cellular fibroma.

readily by cutting and retracting the adjacent ribs until sufficient exposure is obtained.

Four years ago I reported before this society a case with anterior removal of an intrathoracic fibrosarcoma which was about half the size of this tumor, but in the same situation. The symptoms were of twenty-four years' duration, which strongly suggested the presence of a benign tumor which had undergone malignant degeneration. The patient was free from symptoms for about a year and a half after operation, when

recurrence developed, and death occurred of a malignant condition two and a half years after the operation. This emphasizes the importance of early diagnosis and operation.

CASE 9.—A man, aged 60, was admitted to the clinic on March 12, 1928. The final diagnosis was a large intrathoracic cellular fibroma of the right side. The chief complaint was of pain in the right part of the chest of three years' duration. About three years before admission the patient first had noticed in the right lower part of the chest, pain which had radiated to the right lumbar region. The pain had been dull at first, had been periodic, but had been progressive and almost constant for the three months before he came to the clinic. He had not had cough

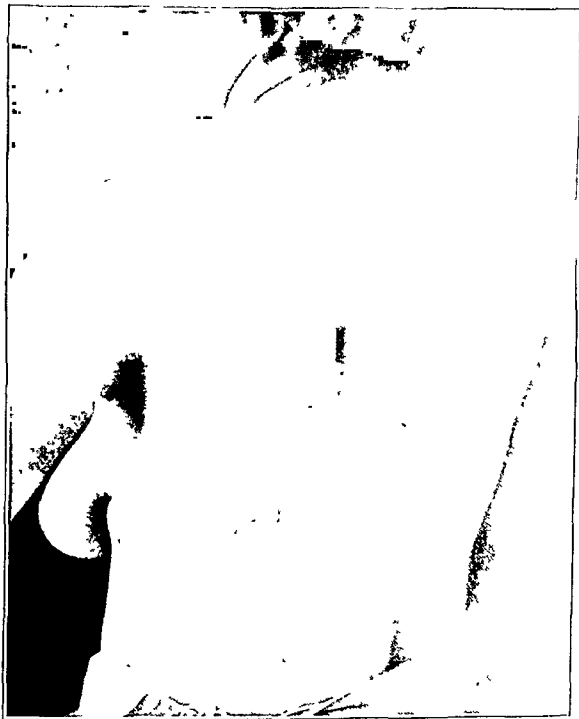


Fig. 26 (case 8).—Wound of left upper posterior mediastinotomy after removal of large intrathoracic tumor weighing 340 Gm. Complete relief from symptoms followed.

or expectoration. There had been marked dyspnea on exertion. Loss of weight had not been noticed. One week previous to admission, the right thoracic cavity had been aspirated and a large amount of bloody fluid had been obtained. A diagnosis of malignant condition of the pleura had been made.

Results of general examination were essentially negative except for decreased breath sounds and dullness to percussion over the posterior lower right part of the thorax. Urinalysis gave negative results. Examination of the blood, including the Wassermann reaction, gave negative results. Roentgenograms disclosed marked increased density of the right lower part of the thorax extending upward

to the level of the second rib. The impression was of intrathoracic tumor, with fluid in the region of the base of the right lung. Fluoroscopic examination showed the diaphragm to be normal in position and function (fig. 28).

Preoperative preparation included right pleurocentesis, with removal of 1,000 cc. of bloody fluid on March 17, 1928. This procedure was repeated on March 28, with removal of 800 cc. of bloody fluid; March 31, with removal of 1,500 cc. of bloody fluid; April 14, with removal of 1,500 cc. of bloody fluid, and on April 18, with removal of 1,200 cc. of bloody fluid. Repeated examinations were made for malignant cells, with negative results, and all fluid sent for culture failed to give a growth.

Right posterior thoracotomy, with removal of about 12.5 cm. of the ninth rib and section of the eighth and seventh ribs at the costovertebral angle, was done

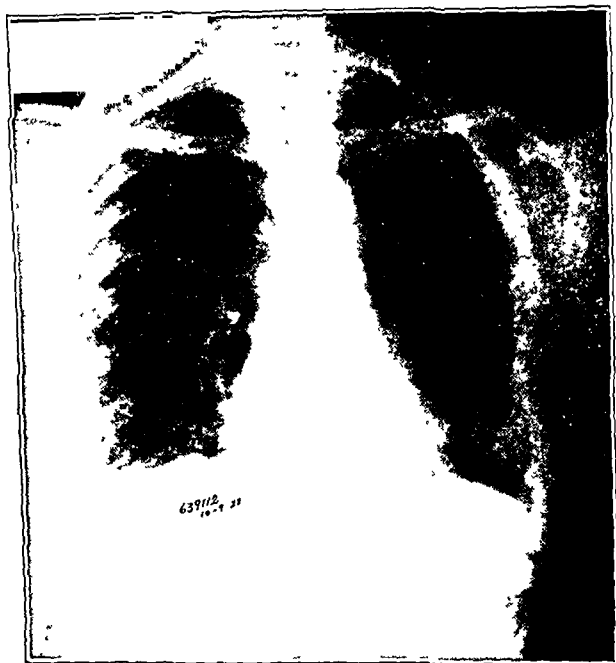


Fig. 27 (case 8).—Roentgenogram taken about six months after transpleural complete removal of tumor and partial resection of the sixth rib and fracture of the seventh, fifth, and fourth ribs on the left. Complete reexpansion of the left lung followed.

April 25. Transpleural complete removal of the tumor was effected. The thoracic cavity was closed without drainage. Intratracheal ethylene and ether anesthesia was used. The right pleural cavity was exposed by incising the pleura along the bed of the partially removed ninth rib. The lower and middle lobes of the right lung were completely collapsed, and there was a large quantity of bloody fluid in the pleural cavity. An elliptical shaped tumor was found filling the entire lower part of the thorax, over which the surrounding middle and lower lobes of the lung were collapsed. The tumor was adherent to the diaphragm as well as to all of the surrounding pulmonary tissue. Dissection by knife was necessary to separate the tumor from the diaphragm and from some parts of the lung. The

tumor also was firmly adherent posteriorly, close to the spine, about the juncture of the tenth rib, and sharp dissection was required at this point. The tumor was completely removed and the pleural cavity was closed (fig. 29).

The operative diagnosis was of intrathoracic cellular fibroma of the lower right part of the thorax, with the tumor arising, apparently, at the juncture of the tenth rib and vertebra. It was adherent to the posterior third of the diaphragm and caused complete collapse of the middle and lower lobes of the right lung to which it was adherent. There was associated bloody pleural effusion. Pathologic examination revealed a cellular fibroma weighing 630 Gm. and measuring 14 by 11 by 10 cm.

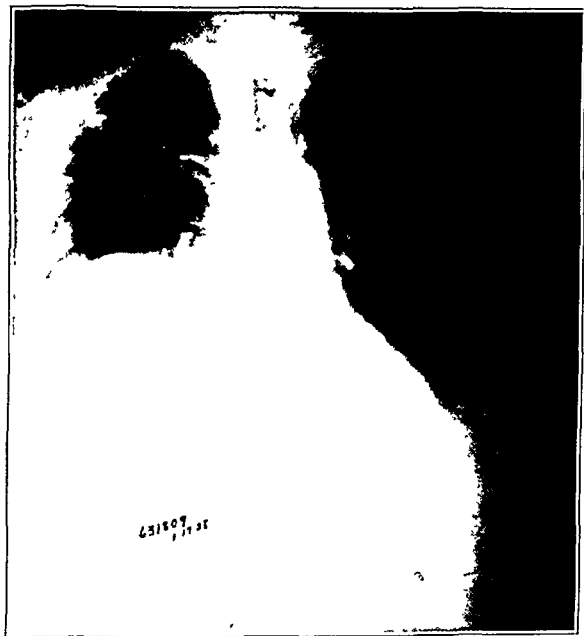


Fig. 28 (case 9).—Roentgenogram taken at time of patient's admission showing marked increased density in right lower thorax to level of second rib, probably an intrathoracic tumor with fluid in right base.

There was moderate shock at the time of operation. On the second day, the temperature was 101 F. and the pulse rate 140. On the fourth day there was a gradual drop of temperature to normal, and of the pulse rate to 110. Fluid was aspirated from the right pleural cavity on the third and sixth days, and on the ninth day a small tube was inserted into the angle of the wound. The cavity was irrigated with a surgical solution of chlorinated soda for a period of three weeks, after which time the tube was removed and the residual pocket was permitted to close by reexpansion of the lung and granulation of the wound. The patient was dismissed in two months from the time of operation. It is now one year since operation; the patient has gained 20 pounds (9 Kg.), and is entirely free from symptoms (fig. 30).

This case is of particular interest because of the age of the patient, and because of the occurrence of a bloody pleural effusion, both of which suggested a malignant lesion. The history of three years' duration and the absence of loss of weight suggested the possibility of a benign lesion, and the patient was placed under observation. The fluid was

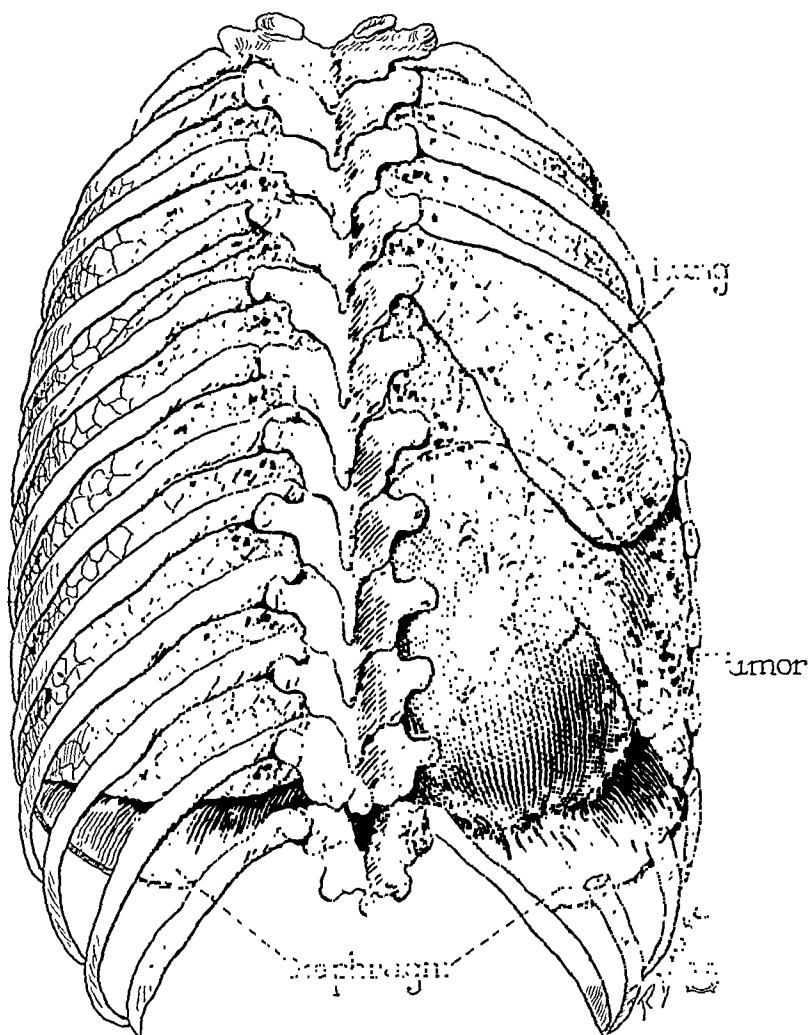


Fig. 29 (case 9).—Large right posterior lower intrathoracic tumor apparently arising at the level of the tenth thoracic vertebra with firm adhesions to the lower lobe of the right lung and diaphragm.

aspirated from the right pleural cavity and a roentgenogram, made immediately after removal of the fluid, showed a large rounded shadow extending above the fluid that remained at the base. This procedure was repeated several times. The removal of the fluid relieved the

dyspnea to a great extent, but did not relieve the pain in the right lower part of the chest. The patient's general condition remained good. It was thought that the tumor was probably benign and operation was advised. Posterior thoracotomy was done, the tumor was removed and microscopic examination showed it to be a fibroma. The immediate convalescence was stormy, but the ultimate result was satisfactory.

This is the only case that I have observed of bloody pleural effusion associated with a benign mediastinal tumor. Intrathoracic operations on patients aged 60 carry great operative risk.



Fig. 30 (case 9).—Resection of the ninth rib; thickened pleura at the right base; lung completely reexpanded; complete relief from symptoms six months after transpleural removal of large intrathoracic fibroma.

CASE 10.—A married woman, aged 38, was admitted to the clinic on April 2, 1929. The final diagnosis was right intrathoracic neurofibroma in the lower right portion of the posterior mediastinum originating at the juncture of the ninth and tenth thoracic vertebrae. The chief complaint was of a dull aching pain in right costovertebral angle. For several years the patient had had attacks of swelling in the right upper quadrant of the abdomen which had lasted from a few minutes to an hour. These attacks had been associated with dull, aching pain at the site of the swelling along the right costal margin. Pain also had been felt at the right costovertebral angle, posteriorly. The pain never had been severe, usually had been more noticeable at night, had been sufficient to keep the patient awake, and on a few occasions after she had been asleep she had been awakened because of the pain. There had been moderate dyspnea on exertion. The patient had not had

cough or expectoration, and there had not been any relationship between the pain and the taking of food. Loss of weight had not been noticed.

The results of general examination were essentially negative. Urinalysis was negative. The combined intravenous phenolsulphonphthalein test of renal function gave a return of dye of 50 per cent. The hemoglobin was 56 per cent and leukocytes numbered 6,400 per cubic millimeter. Slight anisocytosis and poikilocytosis was present. The Wassermann reaction of the blood was negative. Analysis of gastric content showed total acidity of 54 and free hydrochloric acid of 26 in terms of tenth normal sodium hydroxide. The total quantity of gastric content was 80 cc. Roentgenograms of the stomach were negative and examination of the gallbladder revealed normal function. Roentgenograms of the thorax disclosed a circumscribed, round tumor in the right posterior part of the thorax, at

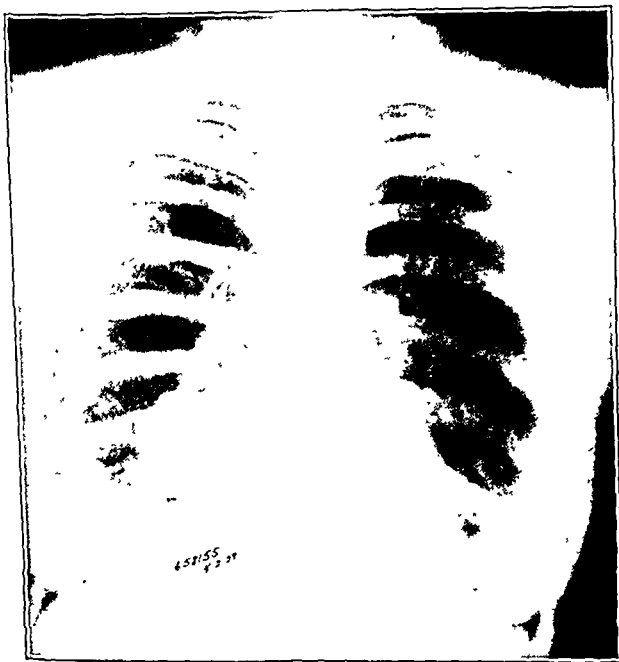


Fig. 31 (case 10).—Round, lobulated, circumscribed tumor in the right lower thorax, posteriorly at the level of the ninth and tenth ribs at time of patient's admission.

the level of the ninth and tenth ribs, posteriorly (fig. 31). The stereoscopic examination showed the tumor to be posterior to the right border of the heart and to the right lung. Fluoroscopic examination showed the tumor to be nonpulsile. Lateral views revealed a rounded tumor in the posterior mediastinum, at the level of the ninth and tenth thoracic vertebrae. The examination of the spinal column disclosed a slight destruction of the right side of the ninth vertebra.

Right posterior thoracotomy, with removal of portions of the ninth rib and section of the seventh, eighth and tenth ribs, was done April 17, 1929. Complete transpleural removal of the posterior mediastinal tumor was accomplished. The thoracic cavity was closed without drainage. There was a large, cystic tumor, 14 by 8 by 6 cm. situated at the level of the ninth and tenth thoracic vertebrae,

posteriorly, and apparently originating at the juncture between these two vertebrae at a point where there was slight erosion of the spinous processes. The tumor extended over the bodies of the vertebrae and forward to the angle of the ninth and tenth ribs. The pleura was under such great tension that the capsule was ruptured during its removal, with escape of about 250 cc. of brownish, clear fluid; this reduced the tumor to about half its original size. The rest of the tumor consisted of solid tissue, and was completely removed, with the overlying pleura. The lower lobe of the lung was partially compressed by the tumor and the surface of the lung was adherent to the diaphragm. After complete removal of the tumor, the cut seventh, eighth and tenth ribs were sutured with double strands of chromic catgut and the incision of the pleura, along the bed of the ninth rib, was closed with plain catgut. The erector spinae muscles were sutured over the angles of the ribs, and the right side of the thoracic cavity was closed. The patient's condition was satisfactory at the completion of the operation. The blood pressure was 105 systolic and 80 diastolic. The pulse rate was 110.

The operative diagnosis was of right intrathoracic neurofibroma situated in the lower part of the posterior mediastinum and originating at the juncture of the ninth and tenth thoracic vertebrae. Pathologic diagnosis was of degenerating neurofibroma.

During the patient's convalescence it was necessary to aspirate the right pleural cavity on several occasions. The first aspiration showed a few colonies of gram-positive cocci on culture, and on the tenth day a tube was inserted into the pleural cavity for drainage and irrigations. There had not been any formation of definite pus, but because of the presence of a daily fever, I thought it advisable to institute intracostal closed drainage. The temperature dropped to normal about four days after insertion of the tube. She has now been dismissed from the hospital and her condition is satisfactory.

CASE 11.—A man, aged 38, was admitted to the clinic on July 14, 1928. The final diagnosis was primary carcinoma of the right lung firmly adherent to the wall of the chest and clavicle and infiltrating into the mediastinum. The chief complaint was pain in the upper right part of the chest, of nine months' duration. The patient had been well until nine months before admission when he first had noticed a sharp pain between the shoulder blades which radiated down the right arm. A diagnosis of neuritis had been made and the chest had been strapped; this had relieved the pain. Five months before he came to the clinic, following exertion, he had noticed the same type of pain throughout the upper part of the chest. This pain had persisted intermittently up to the time of his admission. Tonsillectomy had been performed under local anesthesia about three months before admission but the pain had not been altered, and since had become severe, particularly at night. The pain at the time of admission was of a burning stinging type, and was situated, at times, in the right upper part of the chest and at other times between the shoulder blades and in the upper part of the right arm. About one month before he came to the clinic he had noticed contraction of the pupil of the right eye, with ptosis of the right lid. It was thought that the symptoms might be caused by a cervical rib and a roentgenographic examination was made which revealed a large tumor in the right upper portion of the thorax. He had lost 15 pounds (6.8 Kg.) during the last three months.

General examination revealed Horner's syndrome on the right side. The right pupil did not dilate when cocaine was administered and the right palpebral fissure was narrower than the left. The right arm was warmer than the left, and the muscular tone in this arm was less than in the left. Dulness was noted over the upper right part of the thorax, between the scapulae, and breath sounds were

impaired. The hemoglobin was 64 per cent and the leukocytes numbered 6,200 per cubic millimeter. The Wassermann reaction of the blood was negative. Roentgenograms of the thorax revealed evidence of a tumor of the upper lobe of the right lung anteriorly, extending to the level of the second rib in front. The tumor was thought to be benign (figs. 32 and 33).

Upper right posterior thoracotomy, with removal of a portion of the sixth rib and section of the fifth and fourth ribs at the costovertebral angle was done July 25, 1928. Transpleural exploration of tumor with removal of a specimen for diagnosis was carried out. Intercostal closed drainage was instituted, with insertion of number 20 French catheter through the ninth intercostal space, in the posterior axillary line. Intratracheal ethylene anesthesia was used. When the pleural cavity was opened, a large tumor was found which involved practically



Fig. 32 (case 11).—Tumor in the upper right lobe anteriorly extending to the level of the second rib in front (benign?) at time of patient's admission.

the entire upper lobe of the right lung. The tumor was centrally situated, with a small portion of pulmonary tissue entirely encircling it. This pulmonary tissue, however, was atelectatic and did not become inflated on inspiration. The tumor was adherent to the posterior thoracic wall, from the first to the fifth ribs, and was adherent to the first rib throughout its entire extent, and to the second rib anteriorly. Because of its infiltration into the thoracic wall, it was thought to be malignant and a specimen was removed from its attachment to the posterior thoracic wall at about the level of the fourth rib. This proved to be an adenocarcinoma of the lung. Because of the marked invasion of both the anterior and the posterior wall of the chest, the tumor was considered to be inoperable. The invasion of the anterior thoracic wall probably produced the Horner's syndrome. The cut ribs were tied with chromic catgut and the incision was completely closed

The operative diagnosis was primary carcinoma involving the entire upper lobe of the right lung, firmly adherent to the upper right part of the thoracic wall, both anteriorly and posteriorly, and involving the lower cervical sympathetic ganglion producing Horner's syndrome. Pathologic examination revealed adenocarcinoma, graded 3.

Immediate convalescence was uneventful and the patient was dismissed from my care on the twenty-fourth day. I was informed, by a letter from the patient's wife, that he died, Nov. 5, 1928. His symptoms had become progressively worse until death.

The relatively short duration of symptoms, the severity of the pain and the rapid evolution of symptoms, with loss of weight, suggested that

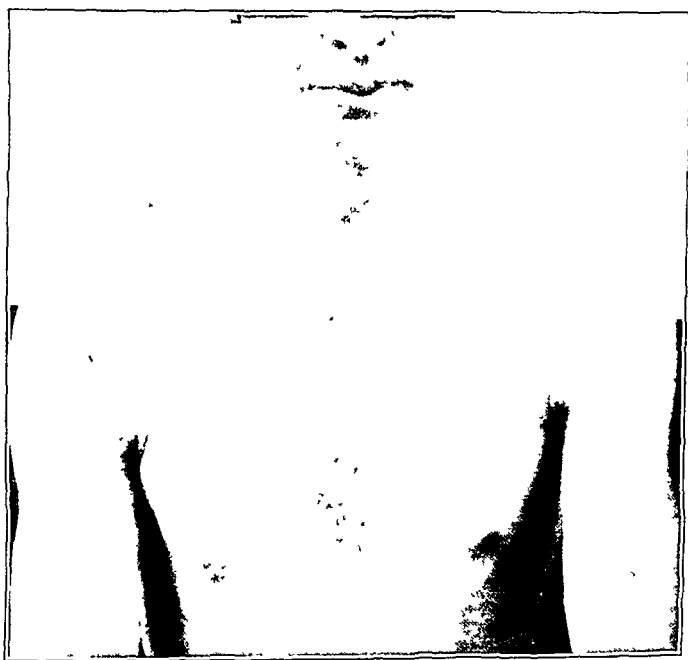


Fig. 33 (case 11).—Horner's syndrome on the right; inoperable primary carcinoma of the upper lobe of the right lung.

the lesion was malignant. The presence of a Horner's syndrome and the fact that a relatively small tumor was shown by roentgenogram, indicated an infiltrating type of lesion. However, the rounded shadow shown by the roentgenogram suggested a possible benign lesion. Operation was advised because of the possibility of the condition being benign and in the hope that if it were malignant it would be sufficiently localized to the upper lobe so that lobectomy would be possible. The tumor was explored through a posterior thoracotomy incision and was found to be an extensive carcinoma of the upper lobe of the lung, infiltrating into the surrounding wall of the chest.

I have operated in three cases of intrathoracic tumor presenting Horner's syndrome at the time of operation. In each instance, the tumor has been malignant; in two cases, it was inoperable, and in the third case, it was removed, but the Horner's syndrome persisted without improvement. This patient died two and a half years after operation from recurrence.

CASE 12.—A man, aged 41, was admitted on June 20, 1927. The final diagnosis was intrathoracic sarcoma attached to the second and third ribs at the articulation with the vertebrae and infiltrating the upper lobe of the left lung, probably originating in the second rib. The chief complaint was of pain in the left part of the chest of six months' duration. Six months before admission, the patient first had noticed pain in the left part of the chest. It had appeared, for the most part, in the evening and had disappeared at bedtime. The pain gradually had increased in frequency and intensity and had been constant for three months previous to admission. It had been situated more in the precordial region and had been sharp and shooting in character, radiating in all directions in the left side of the chest. It had become worse with the patient sitting or standing without support to the chest, as in reclining or leaning against the back of a chair. The pain had been more severe on deep breathing. Following an attack of influenza one year previously, the patient had had persistent cough and blood-streaked sputum. Tuberculosis had been diagnosed and he had been sent to Colorado, where he had been informed that the condition was not tuberculosis. Soon after he had gone to Colorado, the coughing and expectoration had ceased and the pain had become more severe. Marked numbness in the left hand, which radiated to the left elbow, had appeared. He had lost 15 pounds (6.8 Kg.) in six months.

The results of general examination were essentially negative, except for increased breath sounds over the upper lobe of the left lung. The hemoglobin was 72 per cent, erythrocytes numbered 4,500,000 and leukocytes 7,600 per cubic millimeter. The Wassermann reaction of the blood was negative. Roentgenograms of the thorax revealed evidence of a tumor in the upper lobe of the left lung, extending to the level of the second rib anteriorly. The tumor was thought to be benign (fig. 34).

Left upper posterior thoracotomy, with resection of 15 cm. of the fourth rib, was done on July 7, 1927. Transpleural removal of intrathoracic tumor was effected. The thoracic cavity was closed without drainage. Intratracheal ether and ethylene anesthesia was used.

The left side of the thorax was opened through a curved incision, extending around the scapula parallel with the spinal column. A portion of the fourth rib was then removed and the pleura was opened through the posterior periosteum of the rib and exploration of the upper part of the thoracic cavity was carried out. A large tumor was found, which was attached at the costovertebral angle posteriorly, at the level of the juncture of the second and third ribs with the spinal column and extending down to the fourth rib. In separating it from its attachment to the ribs and vertebrae, the capsule was ruptured. It contained broken-down granular tissue which was soft and could be scooped out with the fingers. The tumor had infiltrated into the upper lobe of the left lung in which it had formed a cavity about 6 cm. in diameter. The cavity was completely filled with this broken-down, granular, necrotic material.

The operative diagnosis was of intrathoracic sarcoma attached to the second and third ribs at the vertebral articulation and infiltrating into the upper lobe of the left lung, probably originating in the second rib. Pathologic examination revealed a sarcoma, graded 3, with many giant cells.

Moderate shock followed the operation. Subcutaneous emphysema was noticed about the chest and neck. On the second day this gradually became more marked, involving the entire chest, neck, face and the arms and extending into the fingers and remained about the same for forty-eight hours. The patient was unable to open his eyes and had some difficulty in swallowing and breathing. During this period oxygen was administered by means of a portable oxygen cabinet and after forty-eight hours the emphysema gradually began to disappear and had entirely disappeared from the face and neck by the ninth day, and from the upper part of the

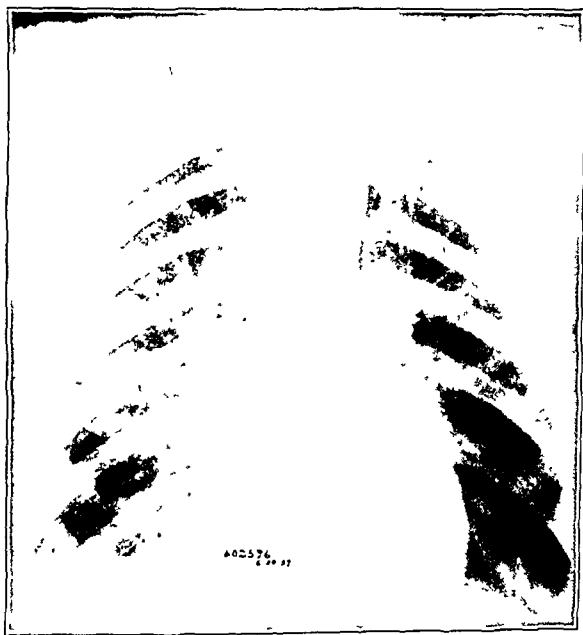


Fig. 34 (case 12).—Tumor of the upper lobe of the left lung extending to the level of the second rib anteriorly (benign?) at time of patient's admission.

chest by the twelfth day. He was dismissed from my care on the fifteenth day after operation, with the wound entirely healed. In reply to a questionnaire sent Jan. 23, 1928, I was informed that the patient had died Oct. 28, 1927.

The short history, and the onset, with severe pain rapidly increasing in severity, and the late development of cough, was more suggestive of a malignant condition than of tuberculosis. The cough probably was the result of the sarcoma infiltrating the lung and causing many small bronchial fistulas. The emphysema following the operation was extensive and probably was caused by the multiple small bronchial fistulas in the bed of the tumor. The condition gradually improved by administra-

tion of oxygen which was continued until the absorption of air permitted normal breathing. Slight surgical emphysema of the tissues around the site of operation on the thorax is not uncommon and rarely persists more than from forty-eight to seventy-two hours.

SUMMARY

Twelve cases of intrathoracic tumors are reported here and five cases have been reported previously. This makes seventeen cases in which transpleural operation has been done.

In fifteen cases the tumor was completely removed, in one case by a two-stage operation and in fourteen cases by a one-stage operation.

In two cases exploration only was performed. The condition was proved to be a high grade malignancy by microscopic examination of tissue removed and the lesion was inoperable because of the extensive infiltration into the wall of the chest and mediastinal structures.

In the entire series of seventeen cases there was one operative death. Death occurred on the seventh day following operation from cerebral embolism. This gives an operative mortality of 5.5 per cent.

The tumor was malignant in eight of the cases, in two of which the tumor was so extensive that exploration only was possible. In the remaining six cases the tumor was removed completely. In two cases, one of malignant endothelioma and one of osteogenic sarcoma, the patients died from metastasis in the first year after operation. One patient with fibrosarcoma died from metastasis two years and two months after operation. Two patients are living. One of these had malignant endothelioma, and a portion of the diaphragm and thoracic wall was resected with the tumor; there is no evidence of recurrence in this case one and a half years after operation. The other living patient had osteofibrosarcoma; there is no evidence of recurrence four years after operation. The remaining patient, who had squamous cell epithelioma, died following operation.

I believe that the operative results in this group of malignant cases justify a more optimistic view than generally is taken in these cases and that they emphasize the importance of early diagnosis.

In the nine benign cases, the tumor was completely removed by an operation in one stage. There was no operative mortality and all patients apparently are cured. It is this group of benign cases that is most gratifying from the surgical standpoint. As it often is impossible definitely to determine the operability, or the type of tumor, by present methods of diagnosis, and, as there is reason to believe that a benign tumor will undergo malignant change as shown in two cases here presented, I believe that in all cases of intrathoracic tumor exploration should be carried out unless the clinical evidence is that a hopeless inoperable condition exists.

THE TREATMENT OF SOME UNUSUAL AND DIFFICULT CASES OF EMPYEMA

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The problem of chronic empyema still presents many difficulties, and there is no standardized procedure applicable to all cases; each must be individualized. I believe, however, that every case of non-tuberculous empyema can be soundly healed by judicious and persistent treatment.

The first step in every long-standing case of pleural suppuration should be a most painstaking study to determine the location and dimensions of the empyema cavity, the expansibility of the lung, the existence of pleurobronchial fistulas and the nature and virulence of the organisms. The general condition of the patient should also be considered in deciding on the extent and type of operation to be undertaken. Most of the patients suffering from long-standing empyema have damaged kidneys and hearts and do not tolerate long and shocking operations. I formerly used Beck's paste to outline the cavity for roentgen study, but since the introduction of iodized oil I have found this medium less toxic and equally efficient. A stereoscopic roentgenogram is taken in the anteroposterior position and one or more in the lateral position.

Many patients come to California and the Southwest with chronic discharging sinuses or wearing drainage tubes in empyema cavities of long standing. These patients are sent in the hope that the climate and life in the open air will heal their chests. They have usually undergone two or three operations and have finally been condemned to wear drainage tubes indefinitely. It is often difficult to gain the confidence of these chronic sufferers and to induce them to make another effort to obtain healing. Many of the cavities will heal promptly if only the tube is removed and left out, but as the patients have worn the tubes for months or years, they are loth to part with them and are often terror stricken at the suggestion.

In addition to the number of cavities that will heal on removal of the tube and daily cleansing of the cavity, there is another large group in which the drainage is poorly placed or inadequate; often there is a residuum of from 4 to 6 ounces (118.4 to 178 cc.) of pus in the bottom of the cavity which drains intermittently or only when the patient is recumbent. A large percentage of these can be healed by adequate dependent drainage and frequent irrigation with surgical solution of chlorinated soda (Dakin's solution).

Before any extensive operation is undertaken to obliterate an old empyema cavity, thorough drainage is secured and the patient's resistance raised by eliminating sepsis. After all the simple measures have been tried, however, and the resistance raised to the maximum, a small group of cases remains which require some radical surgical procedure. I wish to report briefly five such cases and to illustrate the method employed in their treatment.

REPORT OF CASES

CASE 1.—A. B., aged 23, came to California with a discharging sinus of three years' duration. The empyema followed pneumonia. It was drained by a simple rib resection. After more than two years of drainage, another operation was performed, five ribs being resected. There was some improvement, but the sinus persisted. The patient came to California hoping to be cured by the climate, and it was then that I first saw him. Roentgenograms taken at this time, after the injection of bismuth paste, revealed a cavity in the posterolateral aspect of the chest, about 6 inches (15.2 cm.) in length and 1 inch (2.5 cm.) in width. It was separated from the partially expanded lung by a dense membrane. The cavity extended upward and downward about equidistant from the constricted opening in the wall of the chest. A second injection of bismuth paste two weeks later showed the cavity almost double the size it was on first examination. When completely filled, foul smelling pus would well up from the bottom of the cavity. Since there was no improvement, operation was decided on.

First Operation.—The ninth, tenth and eleventh ribs were resected in the posterior axillary line, exposing the bottom of the cavity which rested on the diaphragm. Great improvement followed this improved drainage, but the sinus continued to discharge after prolonged drainage and irrigation with surgical solution of chlorinated soda. After six months' treatment, a second operation was done.

Second Operation.—The cavity was exposed by resection of the previously removed ribs. The thickened pleura was excised, and dense bands of adhesions were divided. The lung was liberated by decortication. All communicating sinuses were obliterated. Prolonged drainage and irrigations with surgical solution of chlorinated soda again failed to secure healing. After eight months the sinuses still persisted.

Third Operation.—The cavity was widely exposed. Decortication of the lung was performed but it would not expand. Two large pedicled skin flaps, one above and one below, were dissected up from the wall of the chest, turned into the cavity and sutured to the thickened visceral pleura; the chest was left widely opened and packed with iodoform gauze. The cavity was packed daily, and rapidly granulated. The skin was pushed in from the edges of the skin flaps, and in about six months the cavity was entirely lined with epithelium. All discharge had ceased, and the patient was restored to perfect health. He has remained well up to the present time, four years after the last operation.

CASE 2.—Dorothy H., aged 23, had pneumonia at the age of 11, followed by empyema. Drainage was performed. The sinus healed and remained closed for one and one-half years, when the cavity refilled; it was again opened. After this operation, it remained healed for three years. The sinus then reopened and has alternately opened and closed at periods varying from three or four months to a year. She had been operated on five or six times with short periods of relief. In 1922, six months before I saw her, after a brief closure, she suddenly

began to expectorate foul pus. She continued to expectorate 8 ounces (236 cc.) daily, with intermittent drainage from a sinus in the left side at the level of the sixth rib. Her general condition was fairly good, but she was harassed by a constant cough and was offensive to every one. Four operations were required to cure her.

First Operation.—The rib was resected at the site of the old sinus. A large empyema cavity was exposed with a Tuffier rib spreader. Thick cicatricial mem-

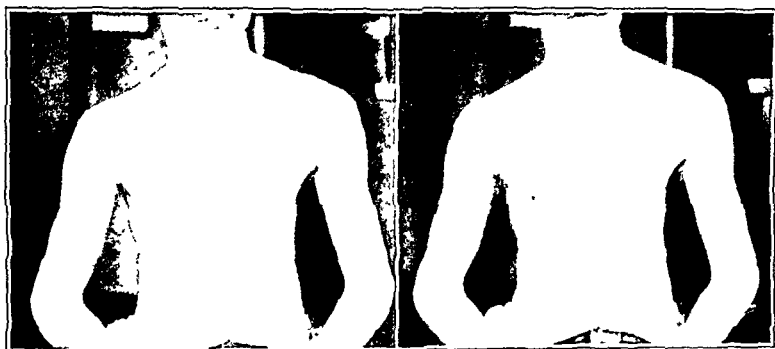


Fig. 1 (case 1).—Chest development after operation, viewed stereoscopically.



Fig. 2 (case 1).—Healed wound, viewed stereoscopically.

brane covering the lung was incised and partially removed, liberating the lung at the site of the pleurobronchial fistula. A pucker string of chromic catgut was placed about the fistulous opening. The pleurobronchial fistula remained closed and the patient's cough ceased, but the empyema cavity continued to discharge. Two months later, another attempt was made to close the sinus.

Second Operation.—Five ribs and the angle of the scapula were resected. The cavity was widely exposed. The thickened pleura was dissected off of the lung as far as possible. The cavity extended up to the apex of the lung and was inaccessible.

Three large pedicled skin flaps were implanted into the bottom of the cavity; the chest was left wide open and packed with iodoform gauze. After the operation, the patient rapidly improved and gained in weight. The cavity was dressed for many months, and it was necessary to do two subsequent operations with implantation of skin flaps to secure complete epithelization of the visceral pleura. The patient has now been well for four years and is pursuing her profession as a teacher of art.

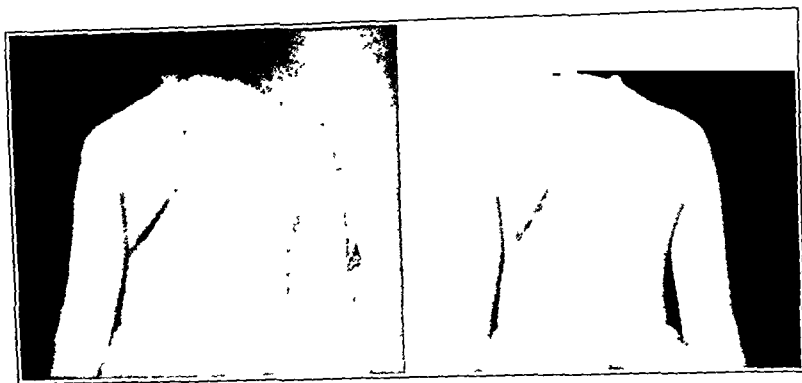


Fig. 3 (case 2).—Incision to reach apex of cavity, viewed stereoscopically.

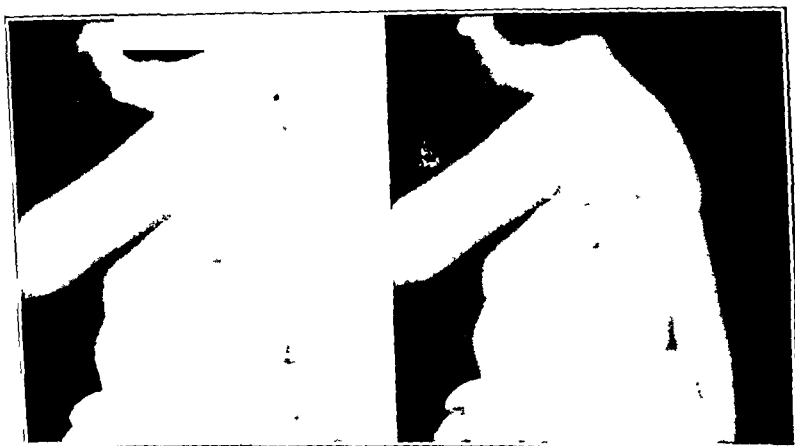


Fig. 4 (case 2).—Healed scar, viewed stereoscopically.

CASE 3.—Mrs. M. C. had empyema secondary to abscesses of the lung. She was referred by Dr. C. C. Browning of Los Angeles for an abscess of the left lung. Six years previously she had suffered from tuberculosis of her right lung, which healed. The development of the abscess can be followed in the x-ray films from its inception until its rupture into the pleural cavity, with the complete filling of the pleural sac with pus. The pus finally broke through into a bronchus, and the patient expectorated from 4 to 6 ounces of fetid pus daily. She was septic and emaciated. The first operation, done in Tucson, Ariz., consisted of

the resection of the eighth rib in the posterior axillary line and the drainage of a thick-walled abscess the size of a hen's egg in the left lower lobe. Improvement followed, but there was a continuous discharge of foul pus, by mouth and through the drainage tube. There were periodic "floodings" of pus, when several ounces would discharge simultaneously through the bronchial fistula by mouth and through the drainage tube. Following these periods, the temperature would drop and the general condition would improve.

Second Operation.—The seventh rib was resected from the costocartilaginous junction to the costovertebral angle. The cavity in the lower lobe was exposed. It was found to consist of several compartments, the uppermost of which communicated by a funnel-shaped opening with a much larger cavity in the upper lobe. The latter occupied almost the entire upper lobe and communicated with a bronchus. These observations explained the periodic floodings of pus. A large



Fig. 5 (case 5).—Front and side views after healing of sinus.

drainage tube was passed through the lower abscess into the upper one, which gave perfect drainage. Rapid improvement followed with greatly diminished expectoration. The sinus of the chest persisted.

Third Operation.—The third operation was performed at the Pasadena Hospital. The lung was freed from the wall of the chest. The fistula was dissected out, swabbed with 2 per cent gentian violet in 70 per cent alcohol and closed with a pucker string of chromic catgut. The chest was closed, with a penrose drain inserted in the posterior angle. The sinus of the chest healed. The patient continued to expectorate 1 or 2 ounces (20 or 60 cc.) of pus daily, with occasional exacerbations of temperature. She regained her normal weight, married and gave birth to a healthy baby. She continued to have periodic attacks of fever with increased sputum. X-ray films taken after the injection of iodized oil revealed a persisting abscess in the left lower lobe

Fourth Operation.—Thoracoplasty was performed, with resection of the fifth to the tenth ribs. The patient has further improved, but still expectorates from 30 to 60 cc. of sputum daily with an occasional rise in temperature. She is practically well and attends to her household duties, but further collapse of the lung will be required to obliterate the old abscess cavity.

CASE 4.—C. F., a man, had interlobar empyema following lobar pneumonia. He first presented a simple effusion which became purulent after two weeks of normal temperature. Closed drainage with a catheter gave temporary relief with normal temperature. In two weeks the temperature again rose to 104 F. X-ray films showed an interlobar collection of pus at the level of the sixth rib. This was drained by resection of the seventh rib in the anterior axillary line. The x-ray film showed the tube in the abscess with a new abscess forming higher up to the inner side of the apex of the lung and near the mediastinum. The temperature, which had dropped to 101 F., again began to rise, and another x-ray picture one week later showed a well developed abscess near the mediastinum.

The eighth rib and a portion of the seventh were resected. The chest cavity was widely exposed so that the hand could be passed up over the apex of the lung to the mediastinal abscess. Two ounces of fetid pus was evacuated, and a large tube introduced. After this operation, the patient improved rapidly; the temperature returned to normal and he made a complete recovery.

CASE 5.—H. L. A., a man, while in the army in France, in 1918, suffered from acute pleurisy with effusion. He recovered from this condition, and after six weeks was sent to the front. He was wounded. Several fragments of shell perforated the right thoracic cavity, and one fragment entered the left pleural cavity. This fragment was thought to have entered the pericardial sac, and a pericardotomy was done. The fragment was found to be posterior to the pericardium. Empyema developed on the right side. This was drained. The patient was in bed for twenty months and was in a critical condition when he was brought back to the United States. Tubercle bacilli were reported to be present in the sputum during his stay in the army hospital. A bronchial fistula developed and drainage continued from a sinus in the posterior axillary line at the level of the tenth rib on the right side. Another sinus anterior and a little above the main one also drained intermittently. On the left side the apex beat of the heart could be seen and felt at the level of the sixth rib, which had been resected. The patient was greatly emaciated and could get about with difficulty. The ribs on the right side from the fifth to the eighth were overlapping, firmly ankylosed and almost perpendicular. X-ray films made after injection of iodized oil into the sinus showed a cavity 2 by 4 cm. communicating with a similar cavity, more external. The iodized oil could be seen entering a bronchial fistula, from which it was aspirated into the left lung which appeared normal.

The fifth, sixth, seventh and eighth ribs, which were ankylosed to one another and to the angle of the scapula, were resected in one piece by means of a Gigli saw. This permitted the cavity to collapse. Both the sinuses and the bronchial fistulas closed promptly and have remained closed. The patient's general condition is much improved.

EMPHYEMA

TREATMENT BY TIDAL IRRIGATION AND SUCTION *

DERYL HART, M.D.

BALTIMORE.

A survey of the treatment for empyema by continuous tidal irrigation¹ and supplementary suction for the past eighteen months² has shown that this method can be used in the presence of practically any type of organism; that it is satisfactory for patients of all ages; that it works best with a trocar thoracotomy but can be adapted for use with patients having a resection of the ribs; that many patients with chronic empyema can be cured without mutilating operations; that bronchial fistulas close within a few days; that the period of convalescence is shortened; that the mortality is relatively low, and that no patient has left the hospital with a draining sinus. The treatment has also simplified the postoperative care, eliminated the difficult and painful dressings, removed the necessity for special exercises and blowing of bottles to give expansion of the lung and chest, and decreased the amount of bacterial soiling in the wards.

METHOD OF TREATMENT

The method of treatment is based on the principle of closed drainage, with the addition of tidal irrigation which is carried on by the normal respiratory movements. The tidal irrigation prevents obstruction of the tube in the majority of cases, thus removing the greatest objection to the closed method. The only fluid that goes into the chest is drawn in by the inspiratory effort. With expiration there is a partial collapse of the thoracic cavity, and the flow of fluid through the thoracotomy tube is reversed. If an opening in the tube is plugged with fibrin during expiration, the reversed flow of fluid with inspiration will wash the obstacle away. The clumps of fibrin are eventually broken up by this motion and are thus evacuated. As the tube should have

* From the Surgical Department of the Johns Hopkins University and Hospital.

* This work was aided by a grant from the Hartley Corporation.

1. Hart, Deryl: *Acute Empyema: Treatment by Continuous Tidal Irrigation and Drainage Dependent on Normal Respiratory Movements*, Arch. Surg. **17**:102 (July) 1928; *Empyema: A Method of Treatment by Tidal Irrigation and Suction with Results Obtained in Thirty Cases*, Internat. Surg. Digest, vol. 7, no. 1.

2. All statistical data are based on the first thirty-five cases except where it is specified that one of the fifteen recent cases, in which the patients are still under treatment or observation, is being discussed.

two or more openings near the inner end, the chance of all becoming obstructed at one time is remote.

In order to carry out the method of treatment, only a reservoir of fluid is needed which has an airtight connection by means of a rubber tube with the empyema cavity (fig. 2). For simplification of the post-operative care, provision can be made for emptying and refilling the reservoir (figs. 1 and 2). Suction can be applied to the empyema cavity by lowering the reservoir, or by lowering the pressure within the reservoir (figs. 1 to 3). In the first cases in which this method of treatment was employed, a rubber bag was used; it was strapped to the abdomen

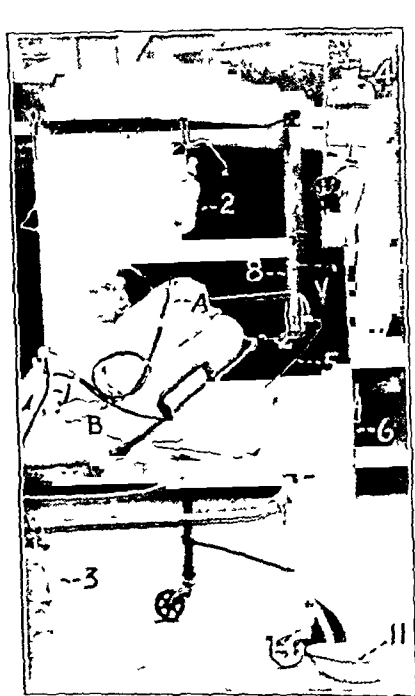


Fig. 1 (patient 16).—Irrigation and suction apparatus used in the treatment for acute empyema complicated by a bronchial fistula.

to give it a dependent position.³ A T-tube was used to connect it with the chest and to make provision for emptying and refilling. This bag was not suitable for use in the presence of a bronchial fistula since there was no way to eliminate the air. A flask with an opening near the bottom was substituted for the rubber bag, and a vent was placed in the top.³ This arrangement permitted the escape of air, or served as a connection for the application of suction as soon as this was desired (figs. 1, 2 and 3). This apparatus can be used on patients with a large thoracotomy wound by covering the opening in the chest with a

3. Hart (footnote 1, first reference).

thin rubber dam through which the thoracotomy tube passes by an airtight connection. Sufficient suction must be maintained at all times to hold the rubber against the chest, thus preventing leakage (figs. 1 and 3).

An apparatus illustrated by figure 4 has been used, and is well adapted to the chronic case in which the cavity is difficult to obliterate. In the more acute cases, irrigation with this apparatus is at times less satisfactory because of the length of the column of water which must be moved to permit the inflow and outflow of fluid. The tendency in this method is toward too rapid obliteration of the cavity, thus causing pocketing. In the chronic case, the cavity cannot be rapidly obliterated, and since this apparatus causes less restriction of the movements of the patient, it is more satisfactory in this type of case. It is possible for patients to be up in a chair as desired without interfering with the irrigations.

In the average case in which this method of treatment is used, there is no leakage from the cavity but only the secretions from the small granulating wound. However, in a few cases limited to small children there was definite leakage, usually beginning from about the seventh to the tenth postoperative day. In two cases the leakage was thought to be due to faulty operative technic, causing bacterial infection and sloughing of the tissues. The wall of the chest of the small child is thin, so that the granulating sinus is short. In most cases, however, the fluid seemed to be pumped out by the respiratory movements. Fluid was drawn in by inspiration, the holes in the catheter were closed at the beginning of expiration, and compression of the cavity by expiration forced the remaining fluid out around the tube. In one case this condition was controlled by inserting a mushroom catheter. No harm has resulted from this leakage. A pad can be placed beneath the patient to care for it. The leakage seldom lasts for more than a few days as the cavity is usually almost obliterated at this time, and it can usually be controlled by a careful regulation of the suction. The incision in the skin through which the trocar is inserted is made sufficiently large so that any leakage about the tube will have an unimpeded outlet to the surface.

In the acute cases, the irrigation was carried on for an average of twenty days. In most cases the irrigation practically stopped within fifteen days, but the apparatus was left in place for from four to seven days longer to give the lung time to become firmly adherent. Otherwise, as soon as suction is released the lung will pull away, the cavity will enlarge and the temperature will rise. In the chronic cases, the irrigation was continued as long as seventy days without leakage. In these cases there was little or no redundant granulation tissue about the opening of the sinus.

ADAPTABILITY OF TREATMENT TO TYPES OF CASES

Age.—The treatment has been found to be satisfactory for patients of any age. However, as already noted, the possibility of leakage around the tube is somewhat greater in small children than in adults. It is unusual for any leakage to occur around the tube in older children or adults.

Duration of Empyema.—The simplest type of patient to treat is the one with massive empyema of sufficiently long duration to prevent an immediate expansion of the lung. In these cases, a moderate amount of suction can be applied from the beginning of the treatment.

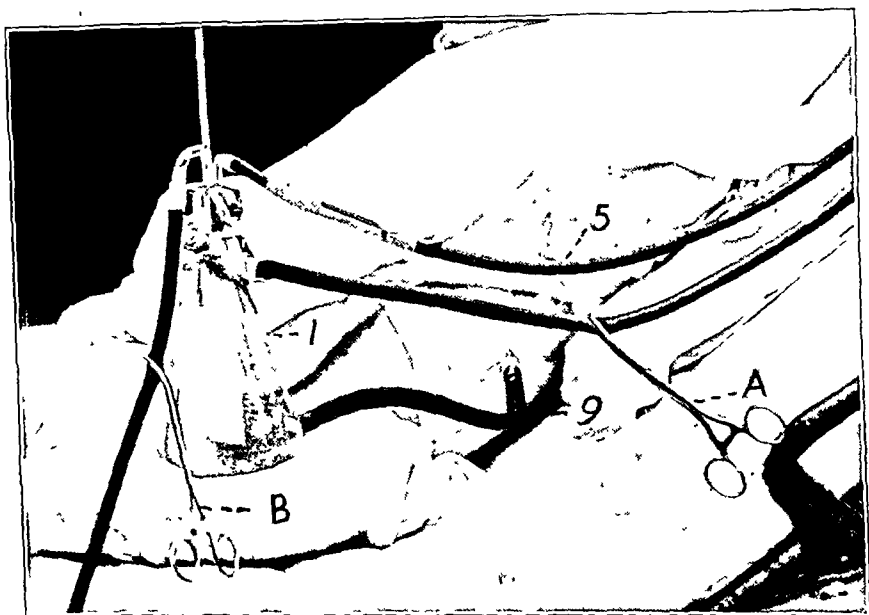


Fig. 2 (patient 16).—A close view of the irrigation flask, 1, and its connecting tubes. Clamp *A* closes the tube by means of which the irrigation flask is refilled from the bottle, 2 (fig. 1), and clamp *B* closes the syphon tube through which the flask, 1, is emptied into the drainage bottle, 3 (fig. 1). The tube, 5, goes to the suction unit (fig. 3), and the tube, 9, goes into the empyema cavity. The latter tube passes through a small hole in a piece of dental dam, an airtight closure is obtained by the contraction of the rubber, and the thoracotomy wound is closed by means of the suction holding the rubber dam against the skin which had been rubbed with petrolatum. A small dressing is placed over the dental dam and the wound. The tube, 9, is longer than was generally used, but even with this length the irrigation is satisfactory. The flask, 1, is suspended so that it will swing with any movement of the patient's body.

With a small amount of suction there is practically no possibility of leakage so long as the tube does not become obstructed. In all cases, however, a period of from a week to ten days should be allowed for

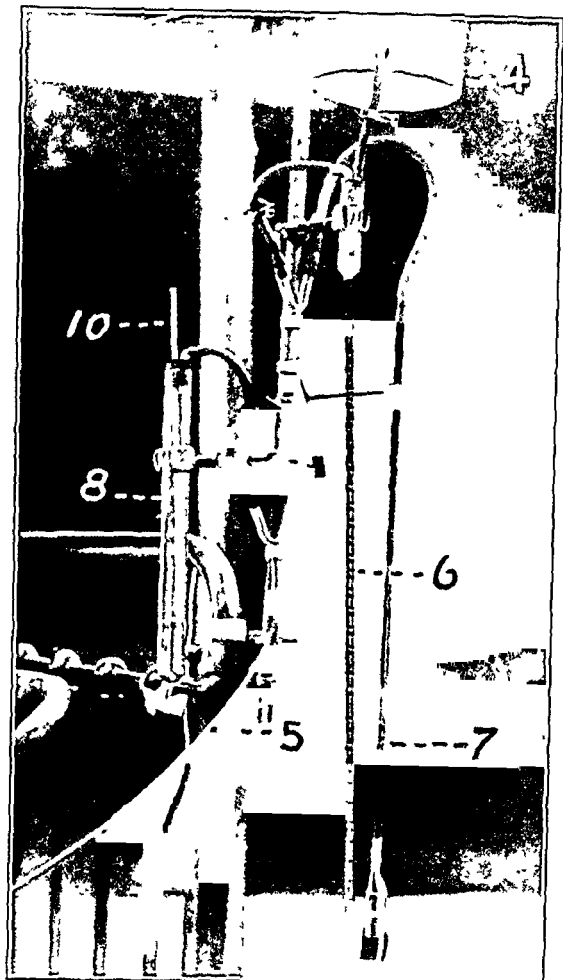


Fig. 3 (patient 16).—The suction unit consists of a Connell apparatus, 4 and 6, with a water manometer, 7, and a reversed mercury manometer, 8 and 10. The suction was obtained by the water dripping from the reservoir, 4, through the upright tube, 6. Air was trapped beneath each drop of water and eliminated from the system. As soon as this elimination exceeded the inflow through any leak, such as a bronchial fistula, suction was obtained. When the pressure within the system plus the weight of the column of mercury in the cylinder, 8, above the lower end of the upright glass tube, 10, was less than atmospheric pressure, air was forced in through the tube, 10, and the mercury. This vent prevented any further increase in the amount of suction as long as the tube, 10, was set at that level, but changing the position of the tube, 10, permitted the accurate regulation of the suction to any desired amount. Whenever the pressure within the system became greater than atmospheric pressure, as when fluid was run in from the bottle, 2 (fig. 1), the air bubbled out through the water manometer, 7, in addition to being eliminated through the tube, 6. Without the valve, 11, the top of which is just visible in figure 1, the Connell apparatus was not satisfactory for suction in these cases. This valve, which was kept beneath the fluid in the drainage pan, permitted the free escape of fluid and air but prevented any back suction with respiratory movements. Otherwise, with the wide excursions of the drops of fluid with respiratory movements, the fluid in each drop would become attached to the side of the tube, destroying the diaphragm effect and permitting air to enter.

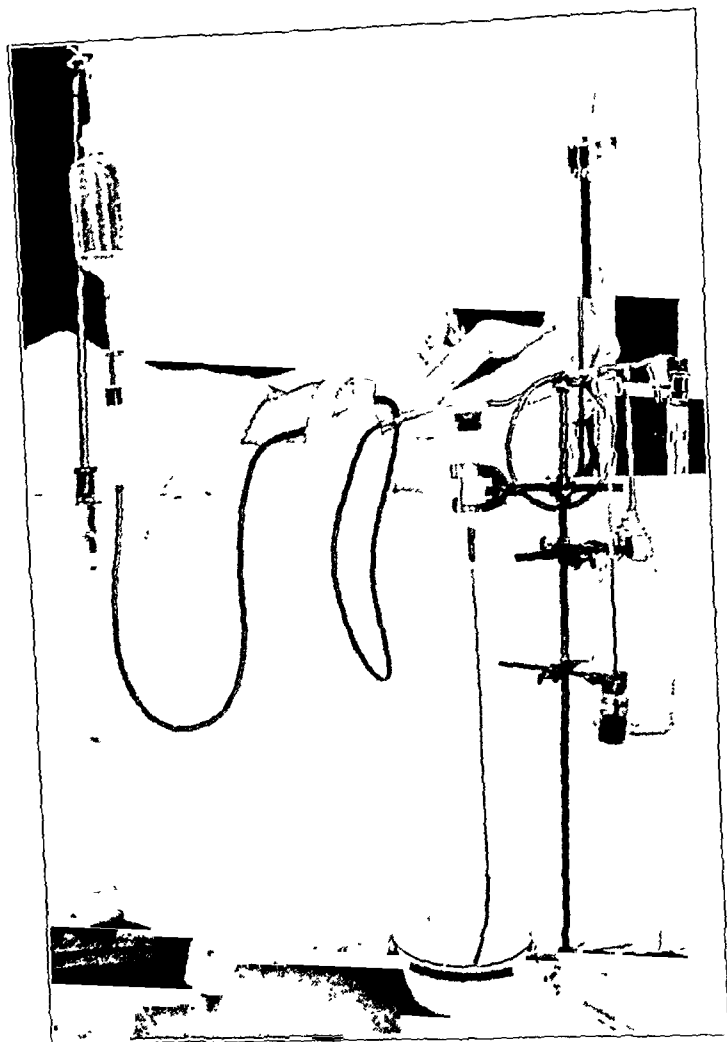


Fig. 4.—A type of apparatus very satisfactory in semichronic cases, but in acute cases it tends to obliterate the cavity too rapidly, thus favoring pocketing. Irrigation is limited because of the length of the column of water which must be moved before the fluid can flow into the chest. Also, if the tube is permitted to hang down as shown in the illustration, the back flow from the waste end during inspiration gives an increasing disproportion between the height of the columns of fluid in the descending and ascending parts of the tube and consequently a rapid increase in the amount of suction. Air is not readily eliminated around this loop, and when it accumulates in the descending tube it may counteract the amount of suction as recorded by the water manometer. A continuous current of fluid down the tube passes back and forth into the chest and any pus is swept down and out. The irrigating fluid drips through the upright tube, and gives suction. The other parts correspond to those in figure 3. The addition of the bottle is to give volume to the system under decreased tension, thus stabilizing suction in the presence of the respiratory movements. The partially concealed tube near the reversed water manometer is added for the connection of a supplementary suction unit if such is available and desirable. The great advantage of this unit in chronic cases is that it does not cause such great restriction to the movements of the patient. At the same time, irrigation is satisfactory since the cavity cannot be rapidly closed, while the slow and forceful respirations carry on an efficient tidal flow.

irrigation without any attempt being made to obliterate the cavity. This delay permits cleansing of the cavity and clearing up of the infection in the granulating wall. The suction is then increased to any desired amount, but it is seldom that more than from 15 to 20 cm. of water is needed, even in the chronic cases of long standing.

In the acute cases, no suction is applied in the early part of the treatment. After the first twenty-four to forty-eight hours, when the sinus is fairly well established and there is less danger of extravasation into the tissues, from 2 to 3 cm. of positive pressure may be used. This slight pressure prevents too rapid obliteration of the cavity, and when there is leakage, this material will find its way out around the tube. When leakage occurs, the positive pressure should be reduced. It is also desirable in these cases to fill the cavity several times a day in order to open up all recesses and prevent any sealing off of pockets until the granulating surface is entirely free from infection. After ten days it is safe to begin the obliteration of the cavity by suction, though it will frequently be almost closed at this time.

In the chronic cases, the cavity is irrigated with surgical solution of chlorinated soda (Dakin's solution) in the early stages to eliminate as much as possible of the redundant granulation tissue. Suction can be applied from the beginning of the treatment, and a larger amount can be used than in the acute cases. Cavities of from eight to twelve months' duration have been obliterated rapidly, and the results suggest that in patients with empyema of much longer standing cure may be obtained by this method, used alone or in association with plastic operations on the wall of the chest.

Condition of Patient.—With a very ill patient, the operation can be performed without taking him from the room or the bed. Two patients have been operated on while in an oxygen tent. Following operation, such a patient is not disturbed by frequent, long and painful dressings. For a patient who is not so ill, provision can be made so that he can sit up in bed or even in a chair. A patient with tuberculous empyema who is now under treatment spends all of his days out of doors in the sun.

Type of Organism and Pus.—The type of organism causing the infection and the character of the pus with which one has to deal make little difference.⁴ With very thin pus the danger of extensive extravasations is greater unless all pressure within the cavity is released.

4. The organisms encountered, with the number of cases of each, are as follows: Pneumococcus, 19 (type I, 3; type II, 3; type III, 1; group IV, 9; not typed, 3); streptococcus, 11 (hemolytic, 7; nonhemolytic, 4, 3 of which were viridans); staphylococcus, 8 (aureus, 6; albus, 1; citreus, 1); colon bacillus, 1; influenza bacillus, 1; diphtheroids, 1.

while some difficulty may arise from obstruction of the tube when the pus is very thick. However, pus which is so thick that difficulty is encountered in aspirating it through a no. 20 French catheter may be gradually worked out by the force of the frequently repeated respiratory movements. An exceptional condition is found when the lung expands quickly so that the parietal and the visceral pleural surfaces are in contact. The cavity in which there is practically no fluid is suddenly flooded with large quantities of exudate which is dislodged from the pleural surface. This sudden release of exudate and fibrin may

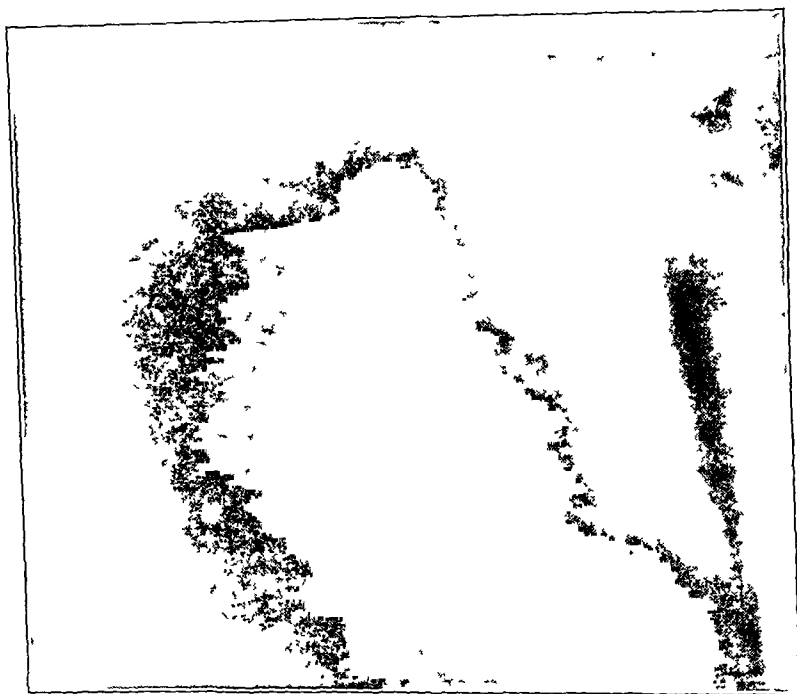


Fig. 5 (patient 16).—Roentgenogram of the chest of a man, aged 26, taken twelve hours after a gunshot wound of the chest and abdomen. In addition to left hemothorax, there was a large abdominal hemorrhage from perforation of the liver and the stomach. Note the marked displacement of the trachea and the heart to the right. Aspiration was done twice, on the third and fourth days, for relief from the respiratory embarrassment. The cultures showed a mixed infection, hemolytic streptococcus, *Staphylococcus aureus* and the colon bacillus being isolated. Trocar thoracotomy was performed on the fifth day.

occur at any time from the first few hours to several days after treatment is instituted, and is most frequent in the cases of pneumococcus empyema.

A certain amount of manipulation may be necessary to evacuate this material. It is best accomplished by running in enough fluid to suspend the solid material and then letting it run out. When the tube is plugged, the material is broken up by a churning force obtained by alternately compressing and releasing the tube. In a few cases this procedure has been necessary, but it never requires more than fifteen minutes and is never needed more than once for any one patient. When the organism is a hemolytic streptococcus, any slight trauma or operation may cause a severe temperature reaction. The patients with staphylococcus

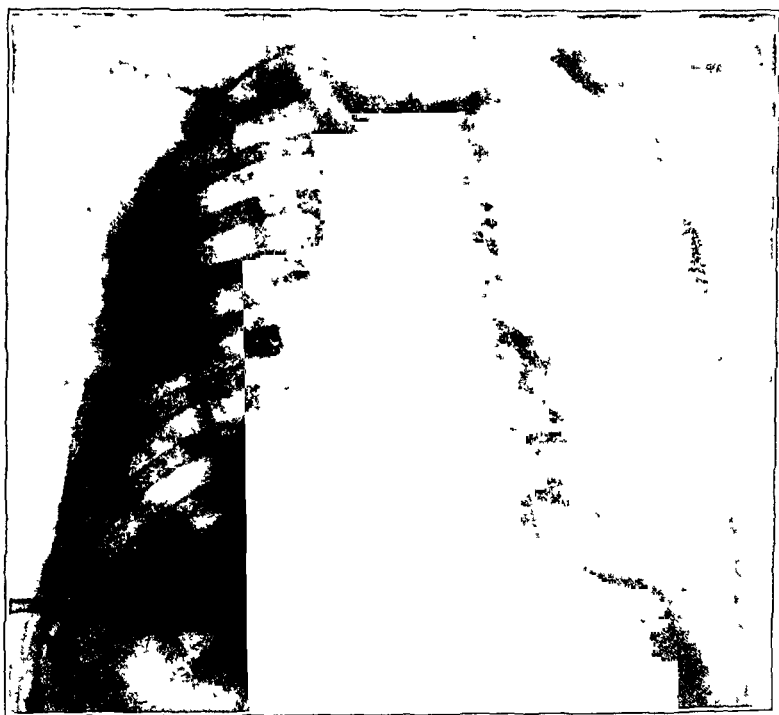


Fig. 6 (patient 16).—Roentgenogram taken forty-eight hours after trocar thoracotomy with the institution of tidal irrigation. For twenty-four hours there had been sufficient leakage of air into the system to suggest a small bronchial fistula. This became much more pronounced, and four days after this roentgenogram was taken a rib was resected in order to obtain dependent drainage (fig. 7). This was necessary because the irrigation system, as used with a rubber bag, became distended with air so that it was unsatisfactory. In the presence of a virulent infection (fig. 11), rib resection was considered necessary as a life-saving measure.

empyema are particularly liable to develop metastatic abscesses (figs. 20 to 23), a complication which occurred in three of these patients, all of whom recovered.

TECHNIC AND RESULTS

Thoracotomy.—In forty-seven of the fifty patients treated up to this time, only trocar thoracotomy has been performed. None has developed an abscess along the drainage tract. A second trocar thoracotomy was performed on four of these patients, only three of whom are included in this report. In one, the first tube was not in the pocket. Two others had more than one pocket, so that the temperature was not reduced following drainage of the first cavity.⁵



Fig 7 (patient 16).—Roentgenogram taken seventeen days after resection of the ribs. On account of the fulminating character of the infection (fig. 11), the resection was more extensive than usual in order to secure absolutely dependent drainage. The temperature soon fell to normal (fig 11), but there was persistent pneumothorax with the left lung completely collapsed and the heart and trachea displaced to the right. There was a large amount of purulent discharge.

It is felt that the manner in which the operation is performed has much to do with the postoperative course. Every effort should be made to place the tube in the most dependent part of the empyema cavity

5. In a patient now under treatment in another hospital, without close personal supervision, the cavity was obliterated too rapidly, and a pocket was walled off posteriorly. Following drainage of this through a trocar thoracotomy, the temperature became normal and improvement has been uninterrupted.

(figs. 4 and 14), and at the same time every precaution taken to cause the minimum amount of trauma and to prevent the extravasation or spreading of pus through the tissues. It is desirable in such a case to have the patient in a moderate to full Fowler's position, both for his respiratory ease in the early stages and for his comfort during the day in the latter part of the treatment. The most dependent part of the chest with this position is about in the midaxillary line. Furthermore, it adds much to the patient's comfort to be able to lie flat on the back

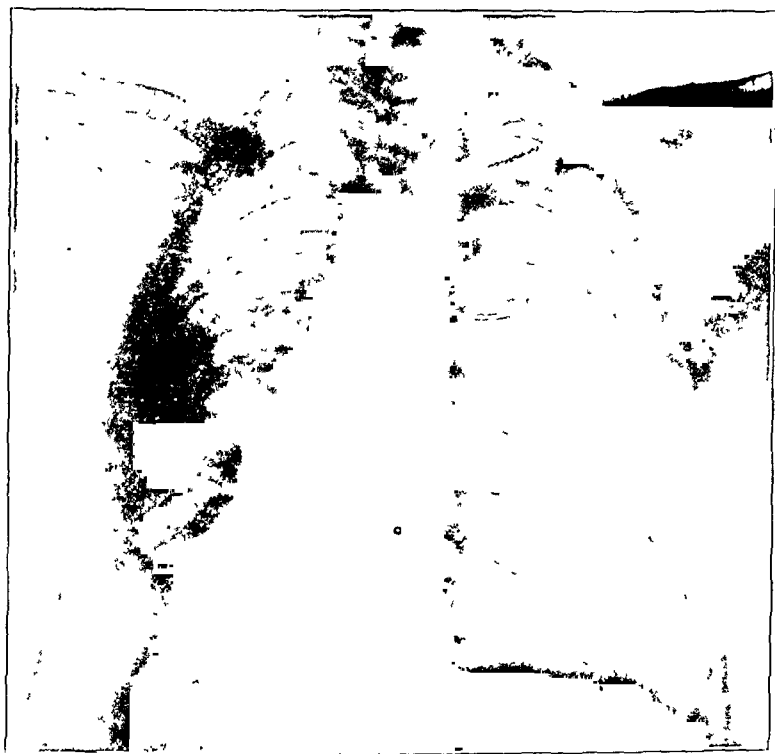


Fig. 8 (patient 16).—Roentgenogram taken three days after that shown in figure 7, and forty-four hours after the institution of tidal irrigation and suction (figs. 1 to 3). The lung has expanded except at the apex and the heart and mediastinum are back to the normal position. There was a moderate rise of temperature (fig. 11), but the patient's general condition was satisfactory. There was considerable pain for the first few days, but after this was over the respirations were normal in rate for the first time following his injury.

without the pain from pressure on a thoracotomy tube. Accordingly, in massive empyema, with the patient lying on the back a line is drawn where the skin comes in contact with the bed, and the thoracotomy is performed just anterior to this line. This assures the patient two com-

fortable positions (back and opposite side), and also insures that the tube will not be obstructed from the pressure of the patient's body (figs. 1, 4 and 17 B).

The point chosen, usually in the eighth interspace, is infiltrated with procaine hydrochloride, care being taken to do all infiltration as the needle is gradually passed in, and to force no fluid out as the needle is withdrawn after it may have become contaminated by piercing the



Fig. 9 (patient 16).—Roentgenogram taken fourteen days after the institution of tidal irrigation and moderate suction in the presence of an open thoracotomy wound. The lung had expanded except for a sinus holding 40 cc., the temperature and respirations were normal, and his general appearance was markedly improved.

infected pleura. At times, when the pus is thin, it is aspirated through this needle, which is left in place. Otherwise the needle is withdrawn, and a larger, aspirating needle is inserted through the periphery of the infiltrated, button-like area. As soon as the needle is between the ribs, determined by palpation, or by "feeling" the rib with the point of the needle, it is directed sharply upward so that the point is kept near the wall of the chest. When the needle is inserted very low, one thus

avoids piercing the stomach, spleen or liver. If pus is not obtained at a depth through which one would feel free to pass the trocar, the needle is withdrawn and inserted in a similar manner one interspace higher. It is unwise to pass the needle to a great depth, strike pus, and withdraw the infected material through uninfected tissue.



Fig. 10 (patient 16).—Roentgenogram taken seventy-two days after the institution of tidal irrigation and moderate suction, for empyema and pneumothorax of twenty-nine days' duration. The patient was discharged from the hospital, entirely cured, thirty-five days after this method of treatment was begun. The wound from the resection of the ribs was completely healed. Note the return of the contour of the chest to normal, with little thickening of the pleura.

When pus is encountered, a sufficient quantity is removed to relieve the marked positive pressure but not to give a negative pressure of any great extent. This procedure insures that the pus will not be forced out around the needle or trocar, leaves a sufficient quantity of pus so that the cavity can be easily entered with the trocar, and avoids too

great a disturbance of the protective wall of granulation tissue. The needle is left in place so that it plugs the hole through which it was inserted. This prevents the extravasation of pus when the patient strains or cries, acts as a pointer indicating the position and depth of the pus, marks the interspace through which to insert the trocar and anchors the layers of the wall of the chest so that the trocar can be passed directly through. The anchoring of the tissues is of the greatest help when the skin is freely movable, or when there is sufficient infiltrated subcutaneous tissue to make palpation of the ribs unsatisfactory.

In the center of the infiltrated area and over the interspace through which the needle passes, a stab wound is made extending through the skin, and of a length corresponding to the diameter of the cannula. The trocar and cannula are now placed with the point in the stab wound, and parallel to the needle, which has been held by the nurse or an

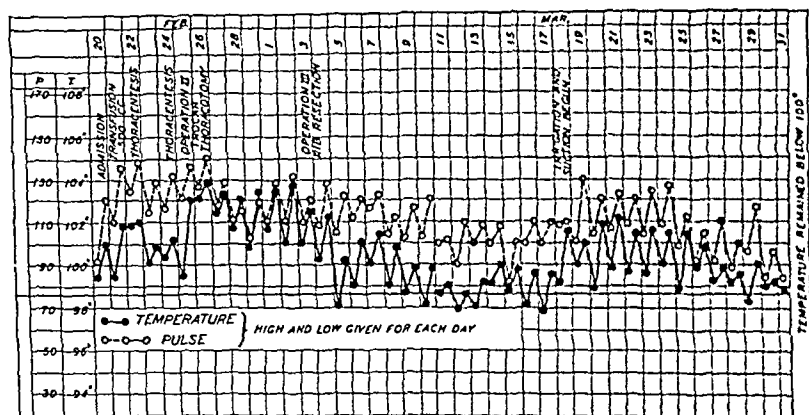


Fig. 11 (patient 16).—Temperature curve showing the rapid pulse and high temperature from the time of admission, and uninfluenced by trocar thoracotomy and tidal irrigation. The closed apparatus with a rubber bag was entirely unsatisfactory in the presence of a bronchial fistula. The temperature quickly fell following resection of the ribs, but with a moderate rise following the too rapid application of suction. This was not alarming, however, and it soon fell and remained normal.

assistant. It is carefully forced into the chest, being stopped as soon as the end of the cannula is within the empyema cavity. This point can be determined by feeling the instrument slide in the cavity as it punctures the pleura as well as by knowing the depth at which pus was first encountered with the needle.

A new catheter, size no. 20 French, with a hole on either side near the tip, marked at a point the length of the cannula from the proximal hole, clamped at the funnel end to prevent the leakage of air, and fitting the cannula so snugly that it must be oiled in order to pass

through it, is now inserted until the mark is even with the outer end of the cannula. This insures that both holes are within the empyema cavity but that the catheter is not inserted so far that it will have to be withdrawn. Any withdrawal increases the chance of spreading the infection into the wall of the chest. The end of the catheter is now placed below the surface of a bowl of warm sterile physiologic solution of sodium chloride, or a funnel (Chetwood syringe without bulb) is attached and partially filled with this solution. The end of the catheter is placed from about 2 to 3 inches (5 to 7.6 cm.) below the level of the thoracotomy wound, and held there until all positive pressure or excess negative pressure is relieved and until it is seen that there is a free tidal flow with respirations. The catheter is clamped at the end of an expiration and held in position, the cannula and the needle are withdrawn and the catheter is again clamped just before it enters the wall of the chest. It is cut off if there is an excess length that is not needed for its attachment to the irrigation apparatus (figs. 2 and 4). After it is connected with the sterile apparatus so arranged that air cannot enter the chest, a small dressing is placed about the tube, and the tube or the apparatus strapped to the body. From this time on the passage between the empyema cavity and the tidal irrigation bag or flask is kept open to avoid any positive pressure within the chest.

Resection of the Ribs.—The two patients⁶ on whom early resection of the ribs was performed, each for massive empyema, present a striking contrast. In the first, the wall of the chest was closed tightly about a large tube and tidal irrigation was used for the first seven days, at which time the wound broke down on account of infection. At that time the cavity had closed to a sinus holding 40 cc., and was estimated as being about the size of the tube. In the second patient, on whom open drainage was used, there was complete left pneumothorax, with the heart and the mediastinum displaced to the right (figs. 5, 6 and 7), seventeen days after the resection of the ribs. It might be argued that the complication of a bronchial fistula was responsible for this condition. However, when the tidal irrigation and suction were adapted to this particular case, there was rapid expansion (figs. 8 to 10), the cavity closing to a sinus holding 35 cc. within fourteen days.

In the presence of the bronchial fistula, the glass flask as a reservoir was used as a basis on which to work (fig. 2). The opening in the chest was closed by placing a dental dam over the skin which had been rubbed with petrolatum. A small opening in the center of the rubber

6. In the third case, one of chronic empyema with a large cavity of eight months' duration, the rib was resected on the thirty-fifth postoperative day for relief from pain caused by pressure of the drainage tube on the intercostal nerve. The cavity held only 35 cc.

dam was stretched until a large tube could be passed through, and with contraction this gave an airtight connection. The entire apparatus with the dental dam about the tube was sterilized, and the tube was inserted through the thoracotomy wound. The dental dam gave an airtight closure of the thoracic cavity as long as sufficient suction was applied to the tidal irrigation flask. In the absence of any other source of suction, the air vent to the tidal irrigation flask was connected with a Connell apparatus (figs. 1 to 3). This was immediately thrown out of commission by the rapid and wide excursions of the drops of water in the upright tube associated with every respiratory movement. The

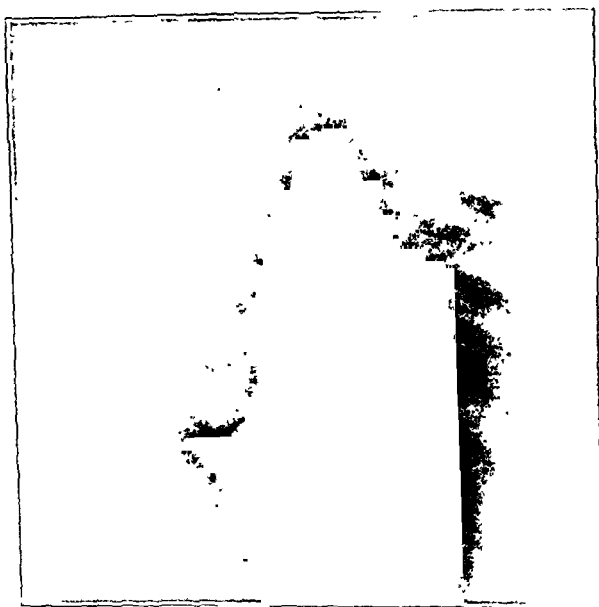


Fig. 12 (patient 12).—Roentgenogram of the chest of a girl, aged 11, taken two days before operation. There is a massive streptococcus empyema of the right side, complicating pneumonia. She was treated by trocar thoracotomy and tidal irrigation at the earliest possible time, and about four days after the probable onset of the empyema. Improvement was rapid and uninterrupted.

lower end of the tube was then placed below the level of the fluid in the drainage basin, and a valve placed on the end, allowing the escape of air and fluid but preventing any sucking back with inspiration. This arrangement adapted the Connell apparatus to this continual variation of pressure, and the apparatus was run sufficiently fast to more than counteract the leakage from the bronchial fistula. If a large bottle is connected so as to increase the volume of the system under decreased tension, it will stabilize the wide variations in pressure associated with the respiratory movements (fig. 4).

A water manometer (figs. 1 and 3, tube 7) was attached so that the amount of suction could be determined at any time. The lung expanded rapidly (figs. 7 to 10) and the fistula closed within thirty-six hours. The reversed mercury manometer (figs. 1 and 3, cylinder 8) was then added to permit the entrance of air when a certain suction was obtained and thus regulate the maximum suction. The long glass tube (10, fig. 3) open to the outside air could be forced to any depth below the surface of the mercury. When the suction was sufficiently great to cause the displacement of the mercury downward for this distance, air would bubble in through the mercury and no greater suction could be obtained.



Fig. 13 (patient 12).—Roentgenogram taken twenty-four hours after trocar thoracotomy for massive empyema on the right side. The heart and mediastinum were displaced to the left (fig. 12). There had been continuous tidal irrigation, with no suction other than that given by the dependent position of the rubber bag. Note the rapid expansion of the right lung, with the return of the heart and mediastinum to their normal position. There was a certain amount of pleural pain associated with the respiratory movements, but no other untoward effects. The temperature rapidly fell to normal (fig 16).

This tube also served, as an entering vent for air when the solution was syphoned from the tidal irrigation flask. Since in most cases not more than from 6 to 8 inches (15.2 to 20.3 cm.) of suction is needed, water is now used instead of mercury. When the flask was refilled all suction was released, but the positive pressure obtained could be no greater than was required to force air out through the water manometer (tube 7, fig. 3) projecting below the level of the colored solution in the small bottle. This was about half an inch of hydrostatic pressure.

In actual use, suction had to be maintained in the empyema cavity at all times. The dental dam was held in position by a small dressing, but the watertight closure was obtained solely by suction. Any temporary release of suction meant an immediate escape of fluid into the bed. Accordingly, while suction was present the tube to the chest was clamped, the tidal irrigation flask emptied and refilled, and only after sufficient suction was present in the system, as indicated by the water manometer, was the tube to the chest unclamped. This apparatus was in use for twenty-seven days, and on only one occasion was there a



Fig. 14 (patient 12).—Roentgenogram taken on the eighteenth postoperative day. Note the marked collapse of the right side of the chest with the slight curvature of the spine. The rapid return to normal can be seen in figures 15 and 17, showing the chest about two months later. The tube is seen in the most desirable position, coming in through the costophrenic angle, and lying along the upper surface of the diaphragm.

leakage of fluid into the bed. This occurred when the Connell apparatus was broken, thus releasing all suction. The tube to the chest was changed every two to seven days in order to remove any secretions beneath the dental dam, and at no time was there any evidence of irritation to the skin. The rapid recovery in this case is told by the illustrations (figs. 5 to 11) and their legends.

Postoperative Course and Care.—*Irrigation:* The reservoir system of irrigation seems to be the more satisfactory. The only fluid that

enters the chest is sucked in by inspiration except for the possible occasional distention of the cavity under slight pressure to discourage any tendency to pocketing. The flask has the advantage over the rubber bag in that it can be used in cases of bronchial fistula, and permits the more accurate regulation of suction. In the early stages the reservoir is emptied and refilled every hour with warm solution, while in the later stages the interval can be lengthened, depending on the amount of drainage. For the first seven to ten days the treatment should be directed toward favoring irrigation rather than collapsing the cavity.



Fig 15 (patient 12) —Roentgenogram showing the complete return to normal, with no deformity (figs 13 and 14), practically no thickening of the pleura and the right costophrenic angle clear without noteworthy adhesions of the diaphragm to the wall of the chest. This roentgenogram was read as "lungs clear. No evidence of old empyema on the right side."

Suction: As soon as the cavity is well cleaned out, the temperature is normal, and time has been allowed for the clearing up of the infection (about ten days), suction can be applied if the cavity is not already obliterated. The simplest method is to place the reservoir below the level of the empyema cavity. In case greater suction is desired, when the rubber bag is being used, the syphon to the floor can be periodically opened for a part of the time. With the rigid walled reservoir this same system of suction can be employed by closing the air vent, or suction can be applied by the elimination of air through the vent in the top

(figs. 1 to 3). Any method which periodically applies and releases the suction is preferable to continuous suction, since the former procedure favors the occasional full distention of the cavity, and thus diminishes the possibility of pocketing. The Connell drip which I use, with provision for regulating the suction, is illustrated in figures 1 to 4.

Obstruction of Tube: The tube became obstructed with pus and exudate in a few cases of pneumococcus empyema on only a few occasions. Obstruction apparently occurred when the lung expanded sufficiently to allow the rubbing off of the thick shaggy exudate on the pleural surface. After this large quantity of exudate which suddenly flooded the cavity was removed, there was no further trouble.

One other cause of obstruction should be noted, however; when the cavity is slow in collapsing, the diaphragm becomes elevated and adhe-

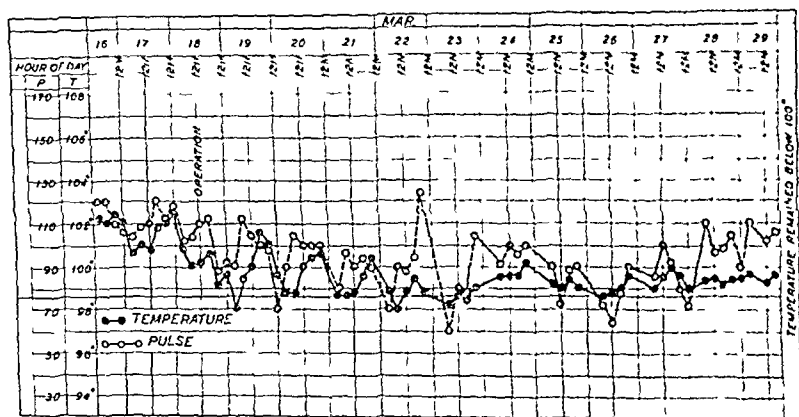


Fig. 16 (patient 12).—Temperature curve showing the rapid fall of temperature to normal within four days after operation. This, together with the course of five other patients having acute hemolytic streptococcus empyema, suggests that delay in operating is not necessary in these cases.

rent to the wall of the chest. When the tube is inserted for only a short distance at the costophrenic angle, it may become closed over, thus preventing drainage and irrigation, a condition which occurred in one of my patients on the thirtieth postoperative day, and the tube had to be inserted to a greater depth before the cavity was entered.

In a number of cases, after expansion occurred, the irrigation completely stopped when the patient lay on the back, indicating that the cavity was collapsed. When the patient was turned on the normal side, however, permitting the weight of the thoracic contents to enlarge the empyema cavity, irrigation immediately began and continued as long as this position was maintained. Early in the treatment of some patients, as much as 500 cc. of fluid ran into or out of the chest when the patient was turned. In a number of cases, after the first week, additional

suction was applied whenever the patient lay with the empyema cavity uppermost. This additional suction facilitated healing by keeping the cavity collapsed and preventing the wide excursion of the wall of the empyema cavity, thus avoiding pulmonary compression and mediastinal displacement.

The index to the collapse of the cavity has been the diminishing excursion of the particles of fibrin which can be seen in the glass connecting tube, *this motion completely ceasing and the drainage becoming thicker when the cavity collapses to a sinus.* From about four to seven

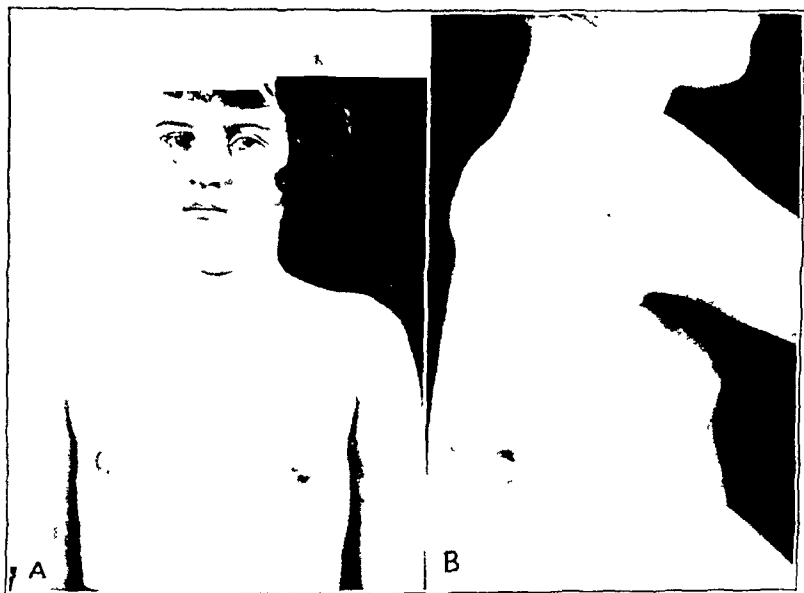


Fig. 17 (patient 12).—*A* was taken eighty-six days after operation. At this time the patient had gained 22 pounds (10 Kg.) in weight, and the chest was entirely normal to inspection and other examinations. *B* was taken four days after the removal of the drainage tube. The sinus was closed except for a small granulating area, and there had been no drainage following the removal of the tube. The scar from the thoracotomy can be seen about in the posterior axillary line, and over the eighth intercostal space. This gave dependent drainage, with the tube lying on the diaphragm (fig. 14), and also permitted the patient to lie on her back without discomfort or obstruction to irrigation.

days after irrigation ceases, the apparatus is disconnected and the tube irrigated. This time is necessary to allow the lung to become sufficiently adherent to prevent a reformation of the cavity by pulmonary collapse. If it is found that when a small amount of fluid is forced into the tube *it comes out through the sinus, the tube is removed and the sinus measured.* This is done by completely emptying the sinus of all fluid and

then filling it until it overflows, the tube being gradually withdrawn as the fluid goes in. This method gives a more accurate estimate of the size of the cavity than do physical or roentgen examinations.

Size of Sinus: For all patients, including those who died about the tenth day, the two with chronic infection of the lung and the one with a resection of the rib in whom irrigation was discontinued on the seventh day, the average size of the cavity at the time the irrigation was discontinued was 9 cc. For the usual case in which trocar thoracotomy



Fig. 18 (patient 1).—Roentgenogram of the chest of an infant, aged 2 months, taken on the sixth day of the empyema, and four days before operation. The empyema was a complication of pneumonia, and the cultures showed *Staphylococcus aureus*. This patient had a bronchial fistula complicating the empyema. She had been treated by periodic aspirations for ten days before operation, and developed multiple abscesses in the puncture wounds (see fig. 19).

was performed and in which the patient went on to recovery, the sinus held from 2 to 6 cc., being practically no more than the space occupied by the tube.

Time Required for Healing after Discontinuance of Irrigation: One of the patients with a chronic infection of the lung had a tube in the sinus for 112 days, the sinus healing within four days after the tube was removed. In the other patient with chronic infection of the lung, empyema of eight months' duration and bronchial fistula, the sinus

healed within seventy days after treatment was started. This saving of time was accomplished by the application of suction until the cavity was completely obliterated. In the other patients who recovered, the tube was kept in for an average of thirteen days after irrigation was discontinued. The sinus promptly healed within an average of five days after the tube was removed, the rapid closing being obtained irrespective of whether the tube had been left in place for a long or a short time.

Dressings: In over 60 per cent of the patients on whom a trocar thoracotomy was performed, the wound was not dressed for the first month except to remove the irrigation apparatus. When the cavity had

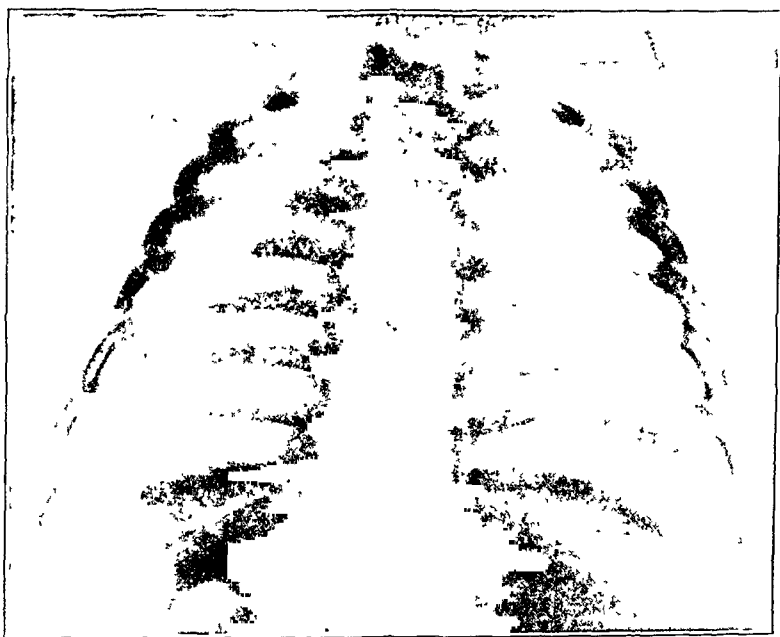


Fig. 19 (patient 1).—Roentgenogram taken forty-four days after trocar thoracotomy. A comparison with figure 18 shows the considerable growth of the patient, the clearing up of all deformity of the chest, and only a slight thickening of the pleura along the axillary border. (Both pictures were taken at 6 feet, and have the same scale of reduction in size.)

closed to a small sinus, the dressings were changed from every one to three days in order to measure the cavity to see that it was not enlarging, and to shorten the tube so as to allow closure from the bottom. In the patients with chronic empyema, dressings, after the first one, were applied from one to two weeks apart. In a patient with tuberculous empyema, the wound was dressed every week in order to cleanse the skin and restrap the apparatus to insure against the tube working back and forth and carrying infection into the chest. In the absence of leak-

age, even after the tube had been in the chest for from twenty to fifty days, there were a number of patients who did not show any redundant granulation tissue about the opening of the sinus (fig. 17 B).

Temperature: The temperature curve is difficult to evaluate on account of the numerous complications, particularly among children. In patients free from other inflammatory lesions, the drop to normal occurred usually within forty-eight to seventy-two hours, and the temperature remained normal throughout the postoperative course (figs. 11, 16 and 22).

COMPLICATIONS

The following list of complications not related to the method of treatment is given as an explanation of the persistent or late elevation of temperature and the consequent delay in removal of the tube: bilateral empyema, 4; pericarditis, 2; peritonitis, 2; septicemia and pyemia, 8; meningitis, 2; pyarthrosis, 1; endocarditis, 1; bilateral pneumonia, 7; chronic infection of the lung, 2; pyelitis, 3; severe infections of the skin (impetigo and furunculosis), 3; bilateral otitis media, 8; acute mastoiditis, 1; diphtheria, 2; diphtheritic myocarditis, 1; measles, 1; mumps, 1; whooping cough, 1; chickenpox, 1; syphilis, 2; acute intestinal indigestion, 1; gunshot wound with perforation of the stomach and liver and severe hemorrhage, 1; bromide delirium, 1.

The complications directly referable to the method of treatment were osteomyelitis of the ribs, 2; enlargement of the cavity following too early removal of suction, 2; severe pain from pressure of the tube on the intercostal nerve, 1. One of the patients now under treatment and not included in this report developed a pocket from too rapid obliteration of the cavity.

Streptococcus Empyema.—Cases of streptococcus empyema are considered separately because in each instance operation was advised and performed at the earliest possible opportunity. This procedure is contrary to a widely prevalent method of treatment, in which operation is delayed as long as possible, the patient being treated by repeated aspirations. The reasons for advising early operation are as follows:

1. The operation is only a slightly more extensive procedure than an aspiration.

2. There is less disturbance to the protective inflammatory zone about the collection of pus if there is a gradual and steady drainage as the lung expands rather than a forced expansion of the lung by a more rapid aspiration. Therefore, it is better to allow a gradual expansion rather than repeated expansions by aspiration, followed by a collapse from the reaccumulation of fluid.

3. There is less danger of abscesses of the wall of the chest that so frequently occur in the puncture wounds.

4. With less trauma to the wall of the chest and particularly to the protective inflammatory zone about the empyema cavity, there is less danger of bacteremia and metastatic infections.

5. Recovery is always favored by the early drainage of pus if this can be done without extensive trauma or the institution of unfavorable conditions, as a sucking wound and pneumothorax.

Of the seven patients with a hemolytic streptococcus infection, six showed immediate improvement (figs. 12 to 17), while the seventh, who had a heavy blood stream infection and signs of peritoneal irritation before operation, died within forty-eight hours. Autopsy showed pericarditis, bilateral empyema and peritonitis.

The four patients with a nonhemolytic streptococcus infection responded well to operation and recovered. One of them, however, had a stormy course due to repeated exacerbations in a basilar pneumonia occurring long after the empyema cavity was completely healed.

Bronchial Fistulas.—Seven of the patients had a bronchial fistula complicating the empyema. Six of the fistulas were of relatively recent occurrence, while one had been present for eight months. All the patients were treated by tidal irrigation, the apparatus used being that with a flask having an air vent to permit the escape of air as it came in through the fistula. With three patients, the flask was kept a little below the level of the empyema cavity to give sufficient suction to prevent aspiration through the fistula (figs. 18 and 19). With the others, including the patient with a resection of the ribs (figs. 1 to 3 and 5 to 11), suction was applied to the contents of the reservoir through the air vent. With this arrangement the flask can be placed at a higher level than the empyema cavity, thus facilitating the escape of air, while the increased height of the flask is counterbalanced by an increase in the amount of suction. In one case the fistula was closed twenty-two hours after operation, in five others forty-eight hours or less after operation, while in the sixth acute case the fistula persisted for four days. The fistula of eight months' duration was closed at the end of a week. With this rapid closure of the fistula, the course of these cases was not unlike that of the cases of simple empyema (figs. 5 to 11, 18 and 19).

Two possible explanations of this rapid closure must be considered: first, that with the expansion of the lung, the sinus through which the leak occurs becomes longer and possibly more tortuous, and therefore the air is less likely to come through, thus giving a better chance of permanent closure. The second, and the one that seems more likely, is that with the expansion of the lung and obliteration of the empyema cavity by adhesions between the parietal and the visceral pleura, the opening into the lung is sealed over by the parietal pleura. These adhesions not only close the fistula, but place the region where it occurred beyond the limits of the empyema cavity.

Complications in Children Two Years of Age and Less (figs. 18 to 23).—There have been twelve patients in this group, five of whom were less than 10 months of age, the two youngest being 4 weeks and 2 months, respectively (figs. 18 and 19). Only one (aged 15 months) died in the hospital,⁷ autopsy revealing a generalized infection and bilateral empyema caused by the influenza bacillus. The condition had been recognized, and drainage obtained on only one side. The mortality over the preceding eighteen years in children 2 years of age and less was 29



Fig. 20 (patient 6).—Roentgenogram of the chest of a girl, aged 2 years, taken thirty-eight days after trocar thoracotomy and eleven days before tidal irrigation was started. (This was the first patient treated with tidal irrigation.) Thirty days after the treatment was begun, the sinus had healed and the patient was ready for discharge.

per cent in the group of patients having a resection of a rib, and in the more recent group in which closed drainage through a trocar thoracotomy was used it was 50 per cent.⁸ Five patients in this age group

7. Another patient, 9 months of age, with a bilateral pneumonia, was removed from the hospital against advice, and is reported to have died at home.

8. Rienhoff, W. F., Jr, and Davison, W. C. Empyema in Infants Under Two Years of Age, *Arch Surg* 17:676 (Oct.) 1928.

with empyema caused by the hemolytic streptococcus have been treated in this hospital. Four died,⁶ while the one treated by tidal irrigation recovered. Of the four patients in this age group with empyema caused by *Staphylococcus aureus*, three developed one or more metastatic abscesses and all recovered (figs. 20 to 23).

ADVANTAGES OF TREATMENT

Free Drainage.—The criticism has been expressed that drainage cannot be as free through a small tube as through the larger opening



Fig. 21 (patient 6).—Roentgenogram taken sixty-eight days after the beginning of tidal irrigation. The patient had been completely well for forty days, and there is now almost no vestige of the empyema.

made by the resection of a rib. I feel that drainage is better with this method of treatment than with resection of a rib, for the following reasons:

1. Every part of the granulating surface is bathed with a relatively clean, nonirritating solution under a tension less than, or certainly not greater than, atmospheric pressure. As long as this fluid has a free circulation with the outside reservoir and as long as it bathes the entire infected surface, there is absolutely free drainage supplemented by continuous washing away of any secretions.

2. When the fluid is under a tension less than atmospheric pressure, the flow of tissue fluids to the surface should be better, and therefore there should be less absorption than when the infected surface is under atmospheric pressure.

3. In all patients who are free from complications and in whom the irrigation is satisfactory, the temperature remains lower (figs. 11, 16 and 22) than in the patients who have a granulating surface wound of equal size. The irrigation of the closed cavity with warm physiologic solution of sodium chloride keeps the wound cleaner and causes less trauma to the delicate protective granulation tissue than do compresses or any type of dressings applied to a surface wound.

Control of Collapse of Lung.—In addition to the satisfactory drainage and absence of the trauma of dressings, there is the additional advantage in the acute cases of having the collapse or expansion of the lung under control. By proper regulation of the amount of suction or of the slight positive pressure in the early stages, the rate of expansion of the lung is under control. Even in the chronic cases of not too long standing the lung can be pulled out to obliterate the dead space. The early obliteration of the cavity, after control of the infection, even by collapse of the wall of the chest and elevation of the diaphragm, is desirable since it stops the formation of scar tissue. Without scar tissue the chest will be restored to its normal size and contour by the action of the muscles of respiration. No exercises are necessary. With a large amount of scar tissue, forming where there is persistent drainage and infection, the deformity will persist and progress despite the additional muscle pull given by exercises and forced breathing.

Rapid Recovery; Absence of Persistent Deformity of the Chest.— With this method of treatment the empyema cavity was usually obliterated within from ten to thirty days, and thus was brought about a rapid recovery without persistent deformity of the chest (see all roentgenograms and photographs of patients). Usually there was an early but marked transient deformity of the chest caused by a curvature of the spine, with a falling together of the ribs and a voluntary splinting of the diseased side (figs. 13 and 14). This condition was particularly common as the rapid expansion quickly brought the pleural surfaces into contact before the formation of adhesions. This contact permitted their rubbing together, with the associated pleural pain and the resultant attempt by the patient to immobilize the chest. It has been noted already that this rubbing together dislodged the exudate over the pleural surfaces. Because of the rapid clearing up of the infection and obliteration of the empyema cavity with the minimal fibrous tissue formation, the chest quickly resumed its normal contour and movements, without any system of exercises. It usually appeared to

be normal by the time the patient left the hospital, and frequently when roentgenograms were taken from two to three months after treatment was begun there was no appreciable thickening of the pleura (figs. 10 and 15).

CONDITION OF PATIENTS AT THE TIME OF AND AFTER OPERATION

The general condition of these thirty-five patients was probably not unlike that of any other group taken at random. Most of them had acute empyema, and were very sick. It was felt that the drainage of any pocket of pus might aid the patient in the fight, so operation was performed as soon as a diagnosis was made, even in the presence of a generalized infection. Naturally, operation on this type of patients tends to increase the mortality rate among the operative cases. Two

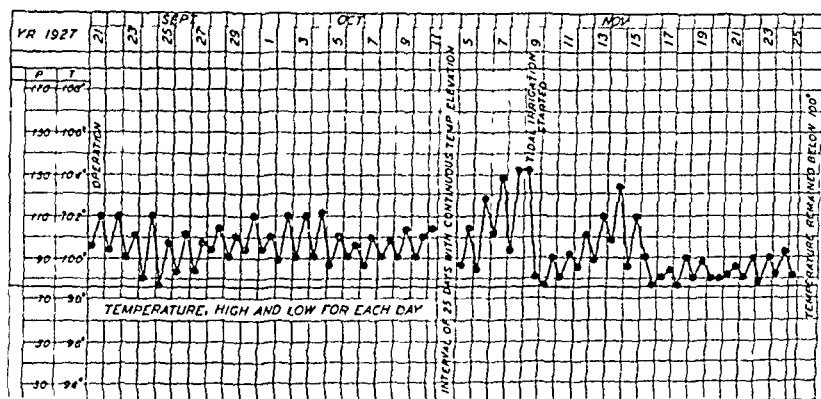


Fig. 22 (patient 6).—Temperature chart showing the continuous fever for forty-nine days, with the drop just at the beginning of tidal irrigation, and the subsequent course with only one rise worthy of note.

of the six patients who died had bilateral empyema and were operated on while in an oxygen tent. Another had ulcerative endocarditis; still another had a heavy blood stream infection and symptoms of peritonitis, the hemolytic streptococcus being the etiologic agent.

Of the patients who recovered, one had bacteremia with a pneumococcus of group IV at the time of operation, and three of the patients with empyema caused by *Staphylococcus aureus* developed metastatic abscesses.

The following notes on chronic and tuberculous empyema are given with a realization that the number of cases is too small to allow the drawing of any conclusions. However, the results to date justify further work along this line of treatment.

Other than a case of tuberculous empyema of one year's duration in which treatment is now being given, the case of longest standing was eight months. This patient had bronchiectasis and a chronic infection of the lung of twenty-five years' standing complicated by a bronchial fistula. The huge cavity healed rapidly, closing to a sinus holding 35 cc. within thirty-five days, and healing was complete within seventy days. In two other cases of ten weeks' and four months' duration respectively, healing was almost as rapid as in the acute cases. The danger of pocketing in cases of long standing is less since the cavity cannot be obliterated in a few hours with the small amount of suction used. The results in these cases have been so satisfactory that I feel that empyema cavities of much longer standing can be obliterated by this method of treatment, and that it can be adapted to use in association with thoracoplasty in the chronic cases of many years' standing. The lung can be expanded as much as possible over a period of weeks or months, and the infection brought under control. Following resection of the ribs, suction can be applied beneath the flap of soft parts, and it will hold the tissues in apposition more satisfactorily than any type of bulky and uncomfortable dressing of pads and adhesive plaster to force the soft parts in. The suction has the great advantage of application to every part of the cavity, both over the lung for expansion and to the wall of the chest for collapse. The irrigation will at the same time remove any discharges from beneath the flap.

No patient who has had either chronic or acute empyema has been discharged with a draining sinus.

Deformity of the chest of a moderate degree persisted in one chronic case. Two other patients, one with acute and the other with chronic empyema, showed in the roentgen examination some elevation of the diaphragm.

In none of these cases was there pocketing within the empyema cavity, and no patient developed an abscess along the drainage tract as the tube was removed.

Osteomyelitis of the rib developed in two patients, in both of whom healing occurred without further operation. In one of these patients a subcutaneous abscess was drained ten months after the empyema. This healed promptly and has given no further trouble.

Of the first thirty-five patients treated, twenty-nine have completely recovered and six have died. (Among the fifteen more recent cases there has been no death, and all the patients are well on the road to recovery.) Since some of the patients who died were in a hopeless condition at the time of operation, a detailed report of each case follows.

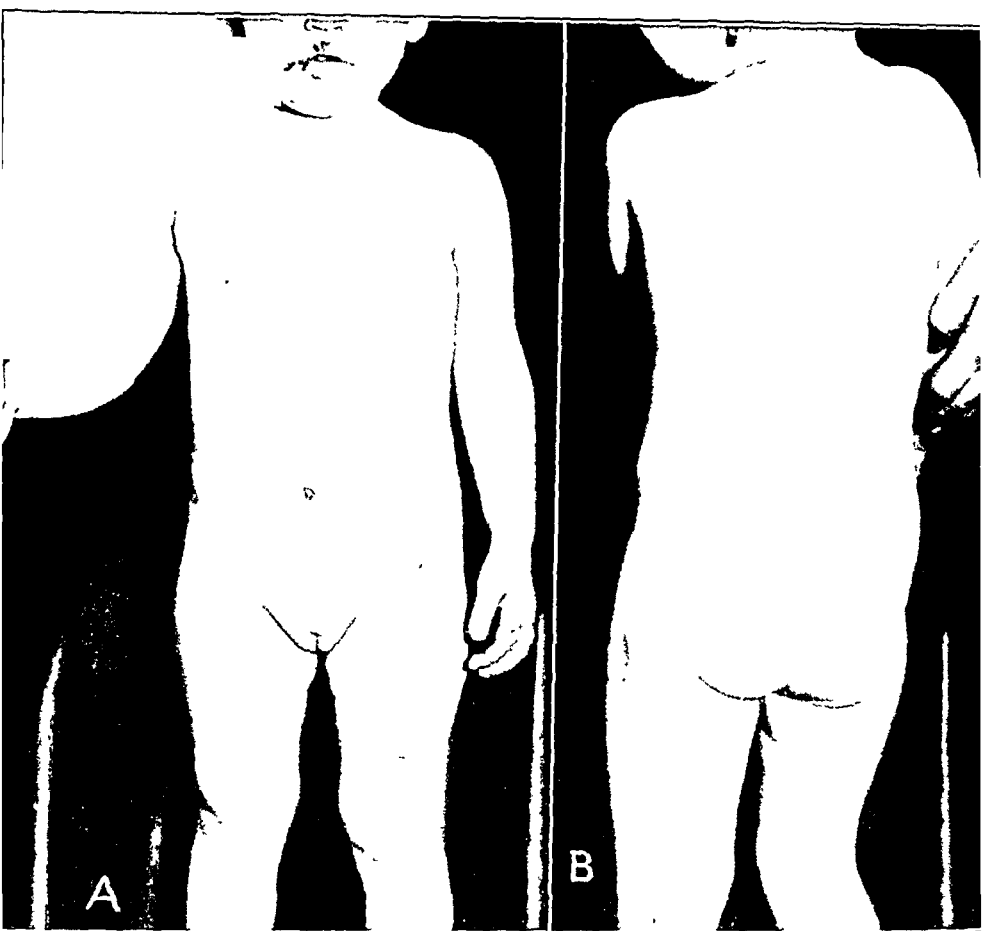


Fig. 23 (patient 6).—*A* was taken six months after the beginning of treatment. The scar on the outer side of the right leg just below the knee can be seen, while one in the left axilla and another on the inner side of the left thigh do not show. *B* shows a larger scar over the left hip. These are the points of incision for the drainage of deep-seated metastatic abscesses which were opened during the course of the empyema. The patient, who had been entirely well for five months, had some digestive disturbance for a few days before the photograph was made. The associated hyperostosis of the ribs is plainly visible. *B* was taken six months after operation, showing the scar from the thoracotomy. A tube in this position prevents the patient from lying on the back or the side; and whenever the patient rolls back, the tube becomes obstructed. The site of the thoracotomy for massive empyema was changed (fig. 17 *B*) to the posterior axillary line, at the most dependent part of the cavity.

REPORT OF FATAL CASES

CASE 1.—A white man, aged 48, with ulcerative endocarditis and septicemia (pneumococcus, type IV) at the time of operation, died on the tenth postoperative day. At autopsy, the empyema cavity was clean, lined by healthy granulation tissue, and held less than 15 cc. The microscopic sections showed little inflammation about the cavity.

CASE 2.—A colored girl, aged 10, with a heavy blood stream infection (hemolytic streptococcus) and symptoms of upper abdominal peritonitis at the time of operation, died forty-eight hours later. At autopsy, the empyema cavity was found to be practically obliterated. There was purulent pericarditis with exudate in the adjacent pleural cavity on either side, diaphragmatic peritonitis and a heavy blood stream infection.

CASE 3.—A white boy, aged 3 years, was described by the pediatricians as moribund at the time of operation for empyema on the left side four days after the right side had been drained. The operation was performed under the oxygen tent. With irrigation of both pleural cavities, with suction to keep the lungs expanded, and with the use of the oxygen tent to relieve the cyanosis and respiratory distress, there was marked improvement. After ten days, the prospect for recovery seemed good. The patient then became rapidly worse, showed signs of extensive fresh pneumonia and died. Permission for an autopsy could not be obtained.

CASE 4.—A colored girl, aged 3 years, with empyema of the right side caused by the hemolytic streptococcus, and complicated by a bronchial fistula, improved rapidly following operation. The fistula closed within twenty-two hours, and the empyema cavity was obliterated to a sinus within three weeks. Three days after irrigation was discontinued, and after three weeks with a normal temperature, the patient developed pneumonia on the left side. This was followed by left-sided empyema (pneumococcus type I). The patient died twelve hours after drainage was instituted, operation having been performed without removing the patient from the oxygen tent. Autopsy showed little pus in the fresh empyema cavity, from which several hundred cubic centimeters had been evacuated. A pericarditis and peritonitis were present, and from these pneumococci, type I, were grown.

CASE 5.—A white girl, aged 2 years, with bilateral pneumonia, was described in the admission note made by the pediatricians as moribund. Contrary to advice, on the ninth postoperative day, her parents, foreign-born and unable to speak English, took her from the hospital. She is reported to have died at home.

CASE 6.—A white boy, aged 1 year, with empyema on the right side caused by influenza bacillus, died on the tenth postoperative day with symptoms of meningitis. Autopsy revealed empyema on the left side which had not been recognized, bilateral pneumonia, pyarthrosis of the right hip and meningitis. The empyema cavity on the right side was small, clean and lined by healthy granulation tissue.

SUMMARY

Tidal irrigation between an outside reservoir and the empyema cavity prevents obstruction of the tube by washing away obstructing particles when the flow is reversed.

No fluid is run into the chest under pressure; fluid is drawn in by the expansion of the chest during inspiration.

Irrigation with a fluid at a tension less than atmospheric pressure, through a system that does not become obstructed, gives a more satisfactory drainage than does an open thoracotomy.

There is less danger of the development of osteomyelitis of the ribs than when the rib is cut across.

The rapidity of lung expansion can be regulated by the amount of suction or slight positive pressure applied.

A report is made of the first thirty-five cases of acute empyema in which continuous tidal irrigation and suction were used.

The patients varied in age from 4 weeks to 48 years, twelve of them being 2 years of age or less.

An initial trocar thoracotomy was performed in all but one of the cases. Two other patients later had a resection of the ribs, one for open drainage in the presence of a bronchial fistula (first case), and the other for the relief from pain caused by contact of the tube with the intercostal nerve.

Of the two patients in whom a rib was resected for drainage, in one the wound was closed tightly about the tube; in the other the opening was closed by rubber dam and suction. In both patients the cavity was rapidly obliterated.

There was a wide variety of organisms, but the method of treatment was equally well suited to all.

The irrigation was equally satisfactory for thick or thin pus. Even coagulated fibrin and exudate came out without obstructing the tube, unless the cavity was suddenly flooded with it.

The empyema cavity was kept cleaner than with any other method of treatment.

The average time of closure to a sinus holding 5 cc. was twenty-one days. The most rapid closure was from a massive empyema cavity to a sinus holding 7 cc. within six days.

Dressings were reduced to the minimum. Frequently there was no dressing from the time of operation until the cavity had closed to a small sinus (thirteen to thirty days).

Leakage about the tube occurred in only an occasional case even when irrigation was continued for from two to three months.

Obstruction to the tube occurred only in occasional cases, and was usually caused by thick exudate which was rubbed off the pleura; in one case it was caused by an elevation of the diaphragm with adhesions to the wall of the chest, thus closing over the end of the tube.

The sinus closed within an average of five days after removal of the tube. No patient has had a draining sinus at the time of discharge.

In uncomplicated cases there was a rapid fall of temperature to normal. Many patients had complications, unrelated to the empyema, causing a febrile reaction. At times this persisted after the empyema had healed, and delayed the final removal of the tube.

The only complication related to the method of treatment was osteomyelitis of the ribs in two cases. No patient developed pocketing⁹ or abscesses along the drainage tract. The other complications were numerous, diverse and often multiple.

Patients with an empyema caused by the streptococcus were treated by early operation; rapid recovery followed with no unfavorable complications due to the method of treatment.

Seven patients had a bronchial fistula, and all recovered as rapidly as those patients with simple empyema. With the expansion of the lung, the fistula closed within the first few days, even one which had been present for eight months.

Of the eleven children 2 years of age or less with whom treatment was followed through, only one died, a mortality of 9 per cent. This rate compares favorably with the average mortality of 29 per cent with resection of a rib and 50 per cent with trocar thoracotomy over the preceding fifteen years.

The results in three cases of chronic empyema have been most satisfactory, and suggest that these cavities of long duration may be obliterated without, or at times in association with, thorocoplasty.

With the rapid recovery there was no persistent deformity of the chest except in one chronic case, and frequently there was not even thickening of the pleura.

Twenty-nine of the thirty-five patients with acute empyema recovered. The six patients⁹ who died had overwhelming infections at the time of operation.

ABSTRACT OF DISCUSSION

ON PAPERS BY LOCKWOOD AND HART

DR. HOWARD LILIENTHAL, New York: There is a slight correction that I must make for the sake of the record. I saw Dr. Lockwood's last patient in France in Base Hospital No. 3. I found him with a very bad empyema, and in a deplorable condition. I tried decortication of the lung, but aeration and expansion did not occur, and I did not dare even to close the wound because the man was in such a perilous condition. The wound was about 14 inches long and wide enough to put two fists into. There he lay, day after day, for weeks, and I could not do another thing for him.

Then I had to leave that base hospital. I came to America, and some months afterward I saw him at the Polyclinic Hospital in New York, which was then an army hospital. He looked about as he did when I left him in France.

I must congratulate Dr. Lockwood for having succeeded in such an unpromising case.

9. To date there have been only these six deaths in over fifty cases.

Dr. Hart's apparatus interested me, but I believe that the simpler suction method of Thiersch is preferable. This is not truly a suction, but an expansion method, and is accomplished by a tube fitted with a rubber valve which prevents the entrance of air into the chest while permitting drainage of fluid and escape of air. Thiersch used a valve made of a rubber dam, but I have found an ordinary slit finger cot will do just as well. The valve is known colloquially as the flapper valve, and I cannot see that there is any great advantage in the rather complicated, extremely ingenious, method which was shown here.

My last case was that of an infant, 6 weeks old, with an acute empyema and abscess of the lungs from which foul pus was discharged by mouth. There was pneumococcus infection. That child was treated by the flapper tube method through an intercostal puncture and was entirely well and discharged from the hospital eleven days from the time of operation.

DR. DERYL HART: I have nothing further to say except in answer to the question as to the type of fluid. In all of the acute cases and some of the chronic cases physiologic solution of sodium chloride was used; in one of the chronic cases a surgical solution of chlorinated soda (Dakin's solution) was alternated with the other solution.

PROCEEDINGS

WEDNESDAY, APRIL 24

The council met in executive session at 8:15 p. m.

THURSDAY MORNING, APRIL 25

The Association met at Barnes Hospital at 9 a. m.

Operative clinics were conducted by Dr. Evarts A. Graham and Dr. Duff S. Allen, St. Louis.

Cases were demonstrated by Dr. J. J. Singer and Dr. Evarts A. Graham, St. Louis.

A short business meeting was held at noon.

THURSDAY AFTERNOON, APRIL 25

Demonstrations were given of recent laboratory work conducted by the staff of Barnes Hospital and Washington University Medical School. Drs. Harry Alexander, William Kountz, Duff S. Allen, Evarts A. Graham, Philip Varney, I. Y. Olch, H. C. Ballou, Peter Heinbecker, S. H. Gray, J. Cordonnier, J. J. Singer, Alfred Goldman and Byron Francis participated.

FRIDAY MORNING, APRIL 26

The meeting was continued in the auditorium of Washington University Medical School. The following papers were presented:

Dr. Emile Holman and Dr. Mary E. Mathes, San Francisco: "The Production of Intrapulmonary Suppuration by Secondary Infection of a Sterile Embolic Area."

Dr. C. M. Van Allen, New Haven, Conn.; Dr. W. E. Adams and L. S. Hrdina, Chicago: "Bronchogenic Contamination in Embolic Abscess of the Lung" and "Embolism in Bronchogenic Infection of the Lung."

Drs. J. B. Flick, Louis Clerf, Elmer H. Funk and John T. Farrell, Jr., Philadelphia: "Pulmonary Abscess: An Analysis of One Hundred Seventy-Two Cases."

Dr. F. A. C. Scrimger, Montreal: "A Case of Abscess of the Lung."

These four papers were jointly discussed by Drs. Willy Meyer, New York; Howard Lilienthal, New York; Wyman Whittemore, Boston; G. P. Muller, Philadelphia; A. L. Lockwood, Toronto; E. F. Butler, Elmira, N. Y.; E. C. Cutler, Cleveland; Kennon Dunham, Cincinnati, and in closing by Drs. Holman, Scrimger, Flick, Clerf and Van Allen.

Dr. Edward D. Churchill, Boston: "Decortication of the Heart (Delorme) for Adhesive Pericarditis."

Drs. John Alexander, A. Garrard Macleod and Paul S. Barker, Ann Arbor, Mich.: "Sensitivity of the Exposed Human Heart and Pericardium."

The discussion on these two subjects was opened by Dr. Evarts A. Graham, St. Louis, followed by Drs. Howard Lilienthal, New York; E. W. A. Ochsner, New Orleans; E. C. Cutler, Cleveland; P. N. Coryllos, New York, and in closing by Dr. Churchill.

Dr. William DeW. Andrus and Dr. J. D. Wilson, Cincinnati: "The Effects of Closed Pneumothorax and Phrenicotomy on the Cardiorespiratory Function."

Dr. Charles D Lockwood, Pasadena, Calif "The Treatment of Some Unusual and Difficult Cases of Empyema"

Dr Deryl Hart, Baltimore "Empyema Treatment by Tidal Irrigation and Suction"

The papers by Drs Lockwood and Hart were discussed by Dr Howard Lilenthal, New York, and in closing by Dr Hart

FRIDAY AFTERNOON, APRIL 26

The Association met in executive session for election of officers, new members and such other business as was brought before the meeting

The following papers were presented

Dr John L Yates, Milwaukee Presidential Address

Dr Howard Lilenthal, New York "Direct Drainage of Tuberculous Pulmonary Cavities"

Dr Edward S Welles, Saranac Lake, N Y "Phrenicectomy in Three Hundred Cases of Pulmonary Tuberculosis"

Dr Ralph C Matson, Portland, Ore "The Electrosurgical Method of Closed Intrapleural Pneumolysis in Artificial Pneumothorax"

Dr Frank S Johns and Dr Dean B Cole, Richmond, Va "Therapeutic Pulmonary Collapse"

These five papers were then discussed by Dr Edward S Welles, Saranac Lake, and in closing by Dr Matson

Drs R H Overholt, George P Muller and Eugene P Pendergrass, Philadelphia "Postoperative Pulmonary Hypoventilation"

This paper was discussed by Drs G P Muller, Philadelphia, Kennon Dunham, Cincinnati, Willy Meyer, New York, Everts A Graham, St Louis, P N Coryllos, New York, J J Singer, St Louis, and in closing by Dr Overholt

SATURDAY MORNING, APRIL 27

The meeting convened at 9 10 a m

The following papers were presented

Dr C C Macklin, London, Ontario "Functional Aspects of Bronchial Muscle and Elastic Tissue"

Dr William Hudson and Dr Hans A Jarre, Detroit "Cin Ex Camera Studies of the Tracheobronchial Tree," with motion pictures

The discussion on these two papers was opened by Dr Everts A Graham, St Louis, followed by Drs Macklin and Hudson, essayists

Dr Stuart W. Harrington, Rochester, Minn "Surgical Treatment of Intrathoracic Tumors"

Dr Pol N Coryllos and Dr George L Birnbaum, New York "The Circulation in the Compressed, Atelectatic and Pneumonic Lung"

Dr Emile Holman, San Francisco, opened the discussion, and Dr Coryllos closed it

Dr James Greenough, Cooperstown, N Y "Operations on the Innominate Artery Report of a Successful Ligation"

The discussion was opened by Dr John Alexander, Ann Arbor, followed by Dr Emile Holman, San Francisco Dr Greenough closed the discussion

Dr Edgar W Phillips and Dr W J Merle Scott, Rochester, N Y "The Surgical Treatment of Bronchial Asthma"

CHANGES IN CONSTITUTION AND BY-LAWS

At the twelfth annual meeting of The American Association for Thoracic Surgery, Article IV, Section 2, of the By-Laws was amended to read as follows:

"Active Membership shall be limited to 100. The candidate, to be eligible, must be resident in the United States or Canada, must be a graduate in medicine of not less than ten years' standing, and must have made a meritorious contribution to knowledge pertaining to the thoracic field. *In unusual circumstances the ten-year requirement will be waived.*"

The amended portion of the section appears in italicized type, and the amendment became effective upon adoption.

LIST OF MEMBERS OF THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

1929

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In Memoriam

HOWARD A. LOTHROP

1864-1928

The American Association for Thoracic Surgery lost one of its most distinguished senior members when Howard A. Lothrop died on June 4, 1928.

He was one of the finest products of the educational institutions of Massachusetts, graduating "magna cum laude" from Harvard College and leading his class, 1891, in the Harvard Medical School. He received the degrees of Master of Arts and Doctor of Medicine. Then, after two years of study in Vienna, he served as house officer at the Massachusetts General Hospital.

Because of the excellence of his scientific work and his ability to impart knowledge, Dr. Lothrop was made instructor in surgery in the Harvard Medical School, in which capacity he served from 1903 to 1912. He was then promoted to the rank of assistant professor of surgery, which he held until 1922. From that time until 1923, he had the honor of being Acting Professor.

Dr. Lothrop was unmarried and lived with his mother, who, with his two brothers and three sisters, survives him.

He retired from the staff of the Boston City Hospital in January, 1927, but retained a large private practice.

His work on the ligation of arteries for aneurysm was one of his important contributions. He was also one of the early contributors to the knowledge concerning epigastric hernia.

Dr. Lothrop had a well deserved reputation as a skilful and conscientious witness in medicolegal accident cases.

His character was lovable and sincere, and his handsome face and youthful carriage made it hard to believe that he was born on Dec. 31, 1864.

Many interests besides medicine and surgery enriched his life. Even as a boy he was interested in natural history and had a fine collection of ornithologic examples of his skill as a taxidermist. He was a musician and had an excellent cultivated tenor voice, to which it was always a pleasure to listen. For many years he was a member of the Harvard Alumni Chorus.

His death was particularly sad. It followed two weeks after the inception of acute septicemia resulting from a safety-pin prick of his

thumb; to add to the tragedy, he was obliged to undergo an amputation of the arm. Such trials demand the highest type of character and fortitude, and Dr. Lothrop faced it all with exemplary courage.

Our Association mourns his loss and extends its deepest sympathy to his family.

NECROLOGY

- 1920 SAMUEL J. MELTZER
LEO S. PETERSON
KENNETH MACKENZIE
- 1921 H. H. JANEWAY
JOSEPH RASONHOFF
ROBERT M. BROWN
ROBERT PATTERSON
- 1922 HENRY L. LYNNAH
- 1923 WILLIAM S. HALSTEAD
- 1927 FRED W. PARHAM
CHARLES H. PECK
SPARRELL S. GALE
- 1928 HOWARD A. LOTHROP

INDEX TO VOLUME 19

	PAGE		PAGE
Abdomen, incision, new.....	129	Arthritis, deformity of knee in.....	759
review of surgery of.....	526	synovial fluid in.....	759
Abscess, embolic, of lungs, bronchogenic		Asthma, bronchial, surgical treatment of....	1425
contamination in.....	1262	Atelectasis: See under Lungs	
embolism in bronchogenic infection of			
lung.....	1279	Bacteria, localization of, in tissues of low-	
of prostate gland.....	1105	ered resistance.....	1086
pulmonary.....	1552	Ballou, H. C.: Celiac plexus and its	
pulmonary; analysis of 172 cases.....	1292	branches.....	399
pulmonary, bacterial flora of treated and		Consequences of variations in mediastinal	
untreated abscesses of lung.....	1602	pressure; mediastinal and subcutaneous	
pulmonary, experimental, following ligation		emphysema.....	1627
of pulmonary artery and incision		Experimental abscess of lung following	
and suture of pulmonary parenchyma.....	1586	ligation of pulmonary artery and incision	
pulmonary, with filling of a cavity and		and suture of pulmonary parenchyma.....	1586
closure of a bronchial fistula by pedicle		Origin of scar tissue in healing of lung.....	1595
muscle graft.....	1313	Barger, J. A.: Carcinoma of colon; intra-	
Achondroplasia.....	754	peritoneal vaccination by mixed vaccine	
Adams, W. E.: Bronchogenic contamination		of colon bacilli and streptococci.....	906
in embolic abscess of lungs.....	1262	Surgical diseases of colon; cooperative	
Embolism in bronchogenic infection of		management.....	518
lung.....	1279	Barker, P. S.: Sensibility of exposed human	
Adrenal Gland: See Suprarenals		heart and pericardium.....	1470
Alexander, H. L.: Emphysema simulating		Barron, M. E.: Thrombo-angiitis obliterans;	
cardiac decompensation.....	1584	general distribution of disease.....	735
Alexander, J.: Sensibility of exposed human		Beaver, M. G.: Variations in extrahepatic	
heart and pericardium.....	1470	biliary tract.....	321
Allen, A. W.: Comparative study of bactericidal		Beck, C. S.: Renal counterbalance.....	673
values of 21 commonly used		Bettman, R. B.: Effect of intrabronchial in-	
antiseptics.....	512	jections of iodized poppy seed oil 40	
Allen, D. S.: Effects of pressure on heart		per cent; study on dogs.....	471
with reference to advisability of decom-		Biliary Tract, bronchobiliary fistula.....	149
pression of greatly enlarged hearts.....	1663	extrahepatic, variations in.....	321
Thoracoplasty and phrenicectomy.....	1545	Birnbaum, G. L.: Circulation in compressed	
American Association for Thoracic Surgery,		atelectatic and pneumonic lung (pneu-	
changes in constitution and by-laws.....	1769	mothorax-apneumatosiis-pneumonia)....	1346
list of members.....	1770	Bladder, cysts of.....	353
neurology.....	1773, 1774	diverticula.....	350
officers of.....	1119	exstrophy.....	354
transactions of.....	1119, 1767	fibrosis of vesical neck.....	354
Amputation, formation of Griggs-Stokes stump		fistula.....	351
operation for making forearm prehensile		mucous glands of.....	355
after loss of a hand.....	769	paralysis.....	352, 1095
Amylase content of blood and pancreatic		stone in.....	349
disease.....	943	stones in children.....	1094
Andrus, W. DeW.: Effects of closed pneu-		surgery.....	1114
mothorax and phrenicotomy on cardio-		tumors of.....	346, 1090
respiratory function.....	1205	Blalock, A.: Oxygen content of blood in	
Report on activities of chest tumor		patients with varicose veins.....	898
registry.....	1121	Trauma to central nervous system; effects	
Anesthesia.....	564	on cardiac output and blood pressure;	
Aneurysm, traumatic, subclavian, arterio-		experimental study.....	725
venous.....	375	Blood amylase estimations in diagnosis of	
Anomalies: See Gallbladder; Kidney; Ureter		pancreatic disease.....	943
Antiseptics, comparative study of bactericidal		diastase in, effect of ligation of tail of	
values of 21 commonly used.....	512	pancreas on.....	788
Appendicitis, acute.....	551	oxygen content of, in patients with varicose	
chronic.....	554	veins.....	898
drainage for.....	553	pressure, trauma to central nervous system;	
in children.....	554	its effects on cardiac output and.....	725
traumatic.....	553	sugar in, improved method for determining	
Appendix, endometrioma of terminal ileum,		ing.....	1116
cecum and.....	152	Bloodgood, J. C.: Osteitis fibrosa and giant	
various positions of.....	554	cell tumor.....	169
Arneson, N.: Value of blood amylase estimations		Bones, carpal, traumatic osteoporosis of..	156
in diagnosis of pancreatic disease.....	943	graft, enlargement of parturient canal by	
Artery, innominate, operations on; report of		growth, damage to, resulting from exposure	
a successful ligation of innominate		to roentgen rays.....	155
carotid and subclavian arteries.....	1484	osteoperiosteal graft, spinal fusion with..	157
		pathologic change in, fundamental conceptions	
		in understanding of.....	760

INDEX TO VOLUME 19

Bones—Continued	PAGE		PAGE
sarcoma, experimental.....	791	Churchill, E. D.: Decortication of heart (Delorme) for adhesive pericarditis.....	1457
structure with particular reference to its fibrillar nature and relation of function to internal architecture.....	24	Chyluria.....	1115
Bowers, L. G.: Pericardotomy for pyopericardium.....	301	Clin-ex camera studies of tracheo-bronchial tree.....	1236
Bradburn, H. B.: Trauma to central nervous system, its effects on cardiac output and blood pressure; experimental study.....	725	Clark, J.: Air embolism from pulmonary vein; clinical and experimental study..	567
Brady, L.: Fibroma of vulva containing epithelial inclusion cyst.....	1061	Clavicle, fracture of.....	162
Branchial Apparatus, its embryologic origin and pathologic changes to which it gives rise; presentation of a familial group of fistulas.....	410	Clerf, L. H.: Pulmonary abscess; analysis of 172 cases.....	1292
Brominized oil, comparison of iodized oil and.....	1660	Cole, D. B.: Therapeutic pulmonary collapse.....	1193
Bronchi, broncho-biliary fistula.....	149	Colon, blood supply of.....	557
bronchial muscle and elastic tissue, functional aspects of.....	1212	carcinoma of.....	555
caliber changes in, in normal respiration.....	1574	carcinoma of; intraperitoneal vaccination by mixed vaccine of colon bacilli and streptococci.....	906
changes in shape and size of tracheo-bronchial tree following stimulation of vagosympathetic nerve.....	1577	diverticulitis of.....	557
comparison of iodized and brominized oils in roentgenology of tracheo-bronchial tree.....	1660	infectious granuloma of.....	558
clin-ex camera studies of tracheo-bronchial tree.....	1236	obstruction of.....	558
effect of intrabronchial injections of iodized poppy seed oil 40 per cent; experimental study on dogs.....	471	surgical diseases of; co-operative management.....	518
Bronchiectasis.....	1559	syphilis of.....	558
Bronchography.....	1571	Colostomy.....	557
Brooks, B.: Surgical applications of therapeutic venous obstruction.....	1	Connor, C. L.: Experimental sarcoma of bone.....	794
Brown, L. T.: Thirty-eighth report of progress in orthopedic surgery.....	153	Contracture, Volkmann's ischemia.....	762
Thirty-ninth report of progress in orthopedic surgery.....	752	Copeland, M. M.: Osteitis fibrosa and giant cell tumor.....	169
Bucholz, C. H.: Thirty-eighth report of progress in orthopedic surgery.....	151	Cordonnier, J.: Early carcinoma of lung.....	1618
Bueermann, W. H.: Review of abdominal surgery.....	527	Coryllos, P. N.: Circulation in compressed atelectatic and pneumonic lung (pneumothorax-apneumotosis-pneumonia).....	1346
Bunions, conservative operation for.....	159	Crohn, N.: Effect of intrabronchial injections of iodized poppy seed oil 40 per cent; experimental study on dogs.....	471
Calcaneum, operation of stripping the os calcis.....	159	Crossan, E. T.: The Delbet apparatus and end-results.....	712
Calcull: See under Bladder; Gallbladder; Kidney; etc.		Cutting, R. A.: Relation of adrenal gland to toxemia of intestinal obstruction; experimental study.....	272
Cancer: See also Sarcoma; Tumor and gastric ulcer.....	519	Cysts, branchial apparatus; its embryologic origin and pathologic changes to which it gives rise, with presentation of a familial group of fistulas.....	410
malignant disease of urinary tract.....	370	epithelial inclusion, found in fibroma of vulva.....	1061
of colon.....	555, 906	of bladder.....	353
of epididymis.....	360	Dandy, W. E.: Loose cartilage from intervertebral disk simulating tumor of spinal cord.....	660
of fallopian tube, primary; 14 cases.....	848	Operative relief from pain in lesions of mouth, tongue and throat.....	143
of lung, early.....	1618	Danforth, M. S.: Thirty-eighth report of progress in orthopedic surgery.....	154
of prostate.....	358, 1101	Thirty-ninth report of progress in orthopedic surgery.....	752
of rectum.....	555	Delbet Apparatus and end-results.....	712
of stomach.....	550	de Takats, G.: Correlations of internal and external pancreatic secretion; effect of ligation of tail of pancreas on diastase in blood.....	788
of testicles.....	360	Correlations of internal and external pancreatic secretion; general considerations and review of literature.....	771
of urethra.....	364	Correlations of internal and external pancreatic secretion; histologic changes in isolated tail of pancreas.....	775
Carbuncle of kidney.....	934	Diastase in blood, effect of ligation of tail of pancreas on.....	788
Carcinoma: See Cancer		Dislocation and fracture of sternum.....	161
Cardiolysis.....	1568	fracture-dislocation of shoulder.....	165
Carpus: See Wrist		intra-articular, of patella.....	769
Cartilage, loose, from intervertebral disk simulating tumor of spinal cord.....	660	living suture grafts in repair of.....	165
Cave, E.: Thirty-eighth report of progress in orthopedic surgery.....	154	of carpal semilunar bone.....	167
Thirty-ninth report of progress in orthopedic surgery.....	752	recurrent, of shoulder.....	766
Cecum, endometrioma of terminal ileum, appendix and.....	152	Diverticula of bladder.....	350
Cellac Plexus and its branches.....	399	of urethra.....	367, 1108
Cholecystography.....	535	Diverticulitis of colon.....	557

INDEX TO VOLUME 19

	PAGE		PAGE
Duodenum, acute complete obstruction of, following gastrojejunostomy; cure by degastro-enterostomy	292	Francis, B. F.—Continued	
hemorrhage from stomach and.....	543	Comparison of iodized oil and brominized oil	1660
Effusions, serous, cytology of, with special reference to tumor cells.....	1672	Consequences of variations in mediastinal pressure; mediastinal and subcutaneous emphysema	1627
Elbow, dislocations and simple fractures of	163	Funk, E. H.: Pulmonary abscess; analysis of 172 cases.....	1292
Elman, R.: Value of blood amylase estimations in diagnosis of pancreatic disease	943	Gallbladder, anomalies.....	535
Embolism, air, from pulmonary vein.....	567	bacteriology of.....	528
and thrombosis.....	561	calculi, acute obstruction of small intestine due to, recovery following operation	915
bronchogenic contamination in embolic abscess of lungs.....	1262	cholecystography	535
in bronchogenic infection of lung.....	1279	disease, etiology of.....	529
production of intrapulmonary suppuration by secondary infection of a sterile embolic area.....	1246	disease in young.....	530
Emphysema, mediastinal and subcutaneous; consequences of variations in mediastinal pressure.....	1627	drainage	533
stimulating cardiac decompensation.....	1584	functions and some of their disturbances.....	1037
Empyema, treatment by tidal irrigation and suction	1732	operations	531
treatment of some unusual and difficult cases of.....	1726	Gallstones: See Gallbladder, calculi	
Endometrioma of terminal ileum, appendix and cecum.....	152	Ganglioneuroma of mediastinum requiring surgical intervention.....	309
Epididymis, carcinoma of.....	360	Gastritis: See under Stomach	
tuberculosis of.....	360	Gastrojejunostomy, acute complete obstruction of duodenum following; cure by degastro-enterostomy	292
Epiphyses, upper femoral, displacement of	753	Genito-urinary tract, tuberculosis of.....	1111
Epispadias	369	Geschickter, C. F.: Osteitis fibrosa and giant cell tumor	169
Epithelium, healing, histologic study of, with practical applications.....	835	Ghormley, R.: Thirty-eighth report of progress in orthopedic surgery.....	154
Ergesterol, irradiated.....	752	Thirty-ninth report of progress in orthopedic surgery.....	752
Esophagus, surgery of.....	53	Gilcreest, E. L.: Traumatic subclavian arteriovenous aneurysm; final report.....	375
Fallopian Tubes, primary carcinoma of; series of 14 cases.....	848	Goiter, old nodular, surrounding trachea posterior to carotid with isthmus posterior to esophagus; case with sudden death from acute abscess.....	466
Farrell, J. T., Jr.: Pulmonary abscess; analysis of 172 cases.....	1292	Goldman, A.: Cytology of serous effusions with special reference to tumor cells.....	1672
Femur, displacement of upper femoral epiphyses	753	Good, L. P.: Ganglioneuroma of mediastinum requiring surgical intervention for relief of obstructive symptoms....	309
fractures of neck of, in childhood.....	768	Graham, A. S.: Lymphatic drainage from peritoneal cavity in dog.....	453
fractures of upper end of.....	164	Graham, E. A.: Clinic demonstrations.....	1552
operative lengthening of.....	764	Effects of pressure on heart with reference to advisability of decompression of greatly enlarged hearts.....	1663
Fibroma of vulva containing an epithelial inclusion cyst.....	1061	Thoracoplasty and phrenicectomy.....	1545
Fingers, fractures of metacarpals and phalanges	767	Value of blood amylase estimations in diagnosis of pancreatic disease.....	943
Fistula, bronchial, closure of, by pedicle muscle graft, in abscess of lung.....	1313	Granuloma, infectious, of colon.....	558
bronchobiliary	149	Gray, S. H.: Early carcinoma of lung.....	1618
of vesical neck.....	351	Greenough, J.: Operations on innominate artery; report of a successful ligation.....	1484
the bronchial apparatus, its embryologic origin and pathologic changes to which it gives rise, with presentation of a familial group of.....	410	Gritti-Stokes stump, formation of.....	167
vesicovaginal	1096	Gynecologist and urologist, necessity for closer relationship between.....	1116
Flick, J. B.: Pulmonary abscess; analysis of 172 cases.....	1292	Halpert, B.: The gallbladder; its functions and some of their disturbances in light of recent investigations.....	1037
Foulds, G. S.: Review of urologic surgery	327, 922, 1090	Harrington, S. W.: Surgical treatment of intra-thoracic tumors.....	1679
Fracture and dislocation of sternum.....	161	Hart, D.: Empyema; treatment by tidal irrigation and suction.....	1732
dislocation of cervical spine, apparatus for reduction of.....	768	Hartwell, S. W.: Surgical wounds in human beings, histological study of healing with practical applications; epithelial healing	835
dislocation of shoulder.....	165	Heart, decompensation, simulated by emphysema	1584
in industry.....	160	decoration of, (Delorme) for adhesive pericarditis	1457
living suture grafts in repair of.....	165		
of clavicle.....	162		
of pelvis.....	163		
of spine.....	162, 768, 968		
ossification after.....	769		
simple, of elbow.....	163		
skeletal traction in treatment of.....	164		
Francis, B. F.: Changes in shape and size of tracheobronchial tree following stimulation of vagosympathetic nerve.....	1577		

INDEX TO VOLUME 19

Heart—Continued	PAGE	Heart—Continued	PAGE
effects of closed pneumothorax and phrenicotomy on respiratory function.....	1205	Kelly, J.: Effect of intrabronchial injections of iodized poppy seed oil 40 per cent; experimental study on dogs.....	471
effects of pressure on heart and advisability of decompression of greatly enlarged hearts.....	1663	Keyser, L. D.: Review of urologic surgery.....	327, 922, 1090
sensibility of exposed human pericardium and.....	1470	Kidneys, anomalies.....	922
surgery (cardiolysis).....	1568	blood supply.....	939
Heinbecker, P.: Caliber changes in bronchi in normal respiration.....	1574	calculi.....	933
Hemangioma, cavernous, of scrotum.....	829	carbuncle of.....	931
Intra-abdominal.....	561	cystic disease of.....	338, 934
Higgins, G. M.: Lymphatic drainage from peritoneal cavity in dog.....	453	function tests.....	371
Hip, congenital dislocation of.....	752	function test, Blanc's phenolsulphon-phthalein test.....	111
paralysis, results of stabilizing.....	765	leukoplakia of renal pelvis.....	871
spontaneous dislocations during early life.....	763	reflexes.....	339
tuberculous, in children, extra-articular fusions of.....	766	removal of, technic for.....	937
Holmann, E.: Production of intrapulmonary suppuration by secondary infection of a sterile embolic area; experimental study.....	1246	renal counterbalance.....	673
Hrdina, L. S.: Air embolism from pulmonary vein; clinical and experimental study.....	567	resection.....	931
Hudson, W. A.: Cin-ex camera studies of tracheobronchial tree.....	1236	surgery.....	1114
Hydronephrosis.....	936	surgical technic.....	327
Hyndman, O. R.: The bronchial apparatus; its embryologic origin and pathologic changes to which it gives rise, with presentation of a familial group of fistulas.....	410	tuberculosis.....	335
Ileum: See under Intestines		tumors of.....	327, 927
Ileus: See Intestine Obstruction		wounds.....	930
Incision, new abdominal.....	129	Kiss, F.: Celiac plexus and its branches.....	399
Infection, localization of bacteria in tissues of lowered resistance.....	1086	Knee, arthroplasty of.....	159
Intestines, endometrioma of terminal ileum, appendix and cecum.....	152	deformity in arthritis.....	739
obstruction, acute complete, following gastrojejunostomy; cure by degastroenterostomy.....	292	Kountz, W. B.: Emphysema simulating cardiac decompensation.....	1584
obstruction due to gallstone; recovery following operation.....	915	Krock, F. H.: Primary carcinoma of fallopian tube; 14 cases.....	848
obstruction; experimental ileus; high obstruction with biliary, pancreatic and duodenal secretions short-circuited below obstructed point.....	1072	Kuhns, J.: Thirty-eighth report of progress in orthopedic surgery.....	154
obstruction; experimental studies on toxicity, intra-intestinal pressure and chloride therapy.....	478	Thirty-ninth report of progress in orthopedic surgery.....	752
obstruction, relation of adrenal gland to toxemia of.....	272	Kummell's Disease.....	162
Iodized Oil, comparison of brominized oil and.....	1660	Kutzmann, A. A.: Leukoplakia of renal pelvis.....	871
poppy seed, 40 per cent, effect of intrabronchial injections of.....	471	Review of urologic surgery.....	327, 922, 1090
Ischemia, Volkmann's: See Contracture, Ischemic		Kyphosis: See Spine, curvature	
Jaffe, H. L.: Structure of bone: with particular reference to its fibrillar nature and relation of function to internal architecture.....	24	Laboratory technic.....	1115
Jarre, H. A.: Cin-ex camera studies of tracheo-bronchial tree.....	1236	Legs, functional importance of equalization of length of.....	156
Jenkins, H. P.: Experimental ileus; high obstruction with biliary, pancreatic and duodenal secretions short-circuited below obstructed point.....	1072	Leukoplakia of renal pelvis.....	871
Joelson, J. J.: Renal counterbalance.....	673	Ligaments, falciform.....	536
Johns, F. S.: Therapeutic pulmonary collapse.....	1193	Light, G.: The bronchial apparatus; its embryologic origin and pathologic changes to which it gives rise, with presentation of a familial group of fistulas.....	410
Judd, E. S.: Review of abdominal surgery.....	526	Lilienthal, H.: Direct drainage of tuberculous pulmonary cavities.....	1161
Review of urologic surgery.....	327, 922, 1090	Linenthal, H.: Thrombo-anglitis obliterans; general distribution of.....	735
		Lockwood, C. D.: Treatment of some unusual and difficult cases of empyema.....	1726
		Lothrop, Howard A., 1864-1928.....	1773
		Lung, abscess.....	1352
		abscess; analysis of 172 cases.....	1292
		abscess, bacterial flora of treated and untreated cases of.....	1602
		abscess, embolic, bronchogenic contamination in.....	1262
		abscess, experimental, following ligation of pulmonary artery and incision and suture of pulmonary parenchyma.....	1586
		abscess, with filling of a cavity and closure of a bronchial fistula by pedicle muscle graft.....	1313
		atelectasis and respiratory failure.....	808
		cancer, early.....	1618
		circulation in compressed, atelectatic and pneumonic lung; (pneumothorax-ap- ulcus cavities.....	1346 1161
		nic infection of.....	1279
		lung.....	1279
		functional aspects of bronchial muscle and elastic tissue.....	1212
		origin of scar tissue in healing of.....	1595

INDEX TO VOLUME 19

	PAGE		PAGE
Lung—Continued		Pancreas	537
postoperative pulmonary hypoventilation	1322	disease of, value of blood amylase estimation in diagnosis of	913
production of intrapulmonary suppuration by secondary infection of a sterile embolic area; experimental study	1246	secretions, internal and external, correlations of	771, 775, 788
suppuration, results of cautery pneumectomy for	1569	Parker, B. R.: Review of abdominal surgery	527
tumors of pleura and	1567	Patella, intra-articular dislocation of	769
Lymphatic System, lymphatic drainage from peritoneal cavity in dog	453	Peliper, H.: Review of abdominal surgery	526
McCann, J. C.: Experimental peptic ulcer	600	Pelvis, contracted, enlarged by bone graft	158
Macklin, C. C.: Functional aspects of bronchial muscle and elastic tissue	1212	fractures of	163
Macleod, A. G.: Sensibility of exposed human heart and pericardium	1470	Pendergrass, E. P.: Postoperative pulmonary hypoventilation	1322
McWhorter, G. L.: Acute obstruction of small intestine due to gallstone; recovery	915	Peptic Ulcer and carcinoma	549
Mason, J. T.: New abdominal incision	129	duodenal and gastric ulcer	542
Mathes, M. E.: Production of intrapulmonary suppuration by secondary infection of a sterile embolic area; experimental study	1246	experimental	600
Matson, R. C.: Electrosurgical method of closed intrapleural pneumolysis in artificial pneumothorax	1175	Pericarditis, adhesive, decortication of heart (Delorme) for	1457
Mediastinum, consequences of variations in mediastinal pressure; mediastinal and subcutaneous emphysema	1627	chronic mediastinal, cardiolysis for	1568
ganglioma of, surgical intervention for obstructive symptoms	309	Pericardium, pericardotomy for pyopericardium	301
Metacarpus, fractures of phalanges and	767	sensibility of exposed human heart and	1470
Monilia, osteomyelitis due to	155	Pericardotomy for pyopericardium	301
Moritz, A. R.: Renal counterbalance	673	Perinephritis	937
Mouth, operative relief from pain in lesions of tongue, throat and	143	Peritoneum, lymphatic drainage from peritoneal cavity in dog	453
Muller, G. P.: Postoperative pulmonary hypoventilation	1322	Peritonitis	559
Muscle, atrophy, experimental study of	168	Perkins, G.: Thirty-eighth report of progress in orthopedic surgery	154
bronchial, and elastic tissue, functional aspects of	1212	Thirty-ninth report of progress in orthopedic surgery	752
riders' leg	764	Perry, M. C.: Intestinal obstruction; experimental studies on toxicity, intra-intestinal pressure and chloride therapy	478
Myofascitis	762	Phalanges: See Fingers	
Nagel, G. W.: Review of abdominal surgery	526	Phenolsulphonphthalein test	1115
Nathanson, I. T.: Correlations of internal and external pancreatic secretion; effect of ligation of tail of pancreas on diastase in blood	788	Phillips, E. W.: Surgical treatment of bronchial asthma	1425
Nerves, sciatic, tests on	770	Phrenicectomy and thoracoplasty	1545
Nervous System, central, trauma; its effects on cardiac output and blood pressure; experimental study	725	in 300 cases of pulmonary tuberculosis	1169
sympathetic, surgery of	756	Phrenicotomy	1193
Neuritis, traumatic ulnar	755	and closed pneumothorax, effect of, on cardiorespiratory function	1205
Nickel, A. C.: Localization of bacteria in tissues of lowered resistance	1086	Pleura and lungs, tumors of	1567
OBITUARIES:		Pneumectomy, cautery in chronic pulmonary suppuration	1569
Lothrop, Howard A., 1864-1928	1773	Pneumolysis, closed intrapleural, electrosurgical method of, in artificial pneumothorax	1175
Och, I. Y.: Experimental abscess of lung following ligation of pulmonary artery and incision and suture of pulmonary parenchyma	1586	Pneumonia, circulation in compressed, atelectatic and pneumonic lung	1346
Origin of scar tissue in healing of lung	1595	Pneumothorax, artificial	1193
Orthopedic Surgery, thirty-eighth report of progress in	154	artificial, electrosurgical method of closed intrapleural pneumolysis in	1175
thirty-ninth report of progress in	752	circulation in compressed, atelectatic and pneumonic lung	1346
Os Calcis: See Calcaneum		closed, and phrenicotomy, effect on cardiorespiratory function	1205
Osteitis fibrosa and giant cell tumor	169	Poliomyelitis	757
Osteochondritis dissecans	155	Porter, M. F.: Old nodular goiter surrounding trachea, posterior to carotid with isthmus posterior to esophagus; case with sudden death from acute abscess	466
Osteomyelitis	759	Prostate Gland, abscess	1105
due to monilia	153	carcinoma of	358, 1101
Osteoporosis, traumatic, of carpal bones	156	hypertrophy	336
Overholt, R. H.: Postoperative pulmonary hypoventilation	1322	hypertrophy, differentiation of 2 types	1097
		Prostatectomy	1099, 1114, 1115
		Pyelonephritis	333
		Pylorus, hypertrophy and stenosis in infants	548
		spasm, in adults	548
		Pyopericardium: See Pericardium	
		Quaintance, P. A.: Fractures of transverse processes of lumbar vertebrae; report of 33 cases	968

INDEX TO VOLUME 19

	PAGE		PAGE
Balke, F.: Intestinal obstruction; experimental studies on toxicity, intraintestinal pressure and chloride therapy.....	478	Stomach—Continued	
Rankin, F. W.: Carcinoma of colon; intra-peritoneal vaccination by mixed vaccine of colon bacilli and streptococci.....	906	hemorrhage from duodenum and.....	543
Surgical diseases of colon; cooperative management.....	518	neoplasms, benign.....	551
Rappaport, I.: Pulmonary atelectasis and respiratory failure.....	808	Ulcer: See Peptic Ulcer	
Registry of Chest Tumors, report on.....	1121	Sugar in urine, improved method of determining.....	1116
Respiration, effect of closed pneumothorax and phrenicotomy on cardiorespiratory function.....	1205	Summers, J. E.: Acute complete obstruction of duodenum following gastrojejunostomy; cure by degastro-enterostomy.....	292
normal, caliber changes in bronchi in.....	1574	Suprarenals, relation of, to toxemia of intestinal obstruction.....	272
Respiratory Tract, pulmonary atelectasis and respiratory failure.....	808	suprarenal-renal heterotopia.....	341
Riders' Leg: See under Muscles		technic for removal.....	938
Rlenhoff, W. F., Jr.: Gross and microscopic structure of thyroid gland in man.....	986	Sutures, living suture grafts in repair of fractures and dislocations.....	165
Riggs, T. F.: Ganglioneuroma of mediastinum requiring surgical intervention for relief of obstructive symptoms.....	309	Synovial Fluid in arthritis.....	759
Roentgen Diagnosis: See also Clin-ex camera bronchography.....	1571	Syphilis of colon.....	558
comparison of iodized oil and brominized oil in.....	1660		
of tuberculosis of spine.....	756	Tendons, spontaneous dislocation and destruction of biceps brachii.....	156
Sager, W. W.: Localization of bacteria in tissues of lowered resistance.....	1086	stenosing fibrous tendovaginitis over radial styloid.....	157
Saint, J. H.: Surgery of esophagus.....	53	transplantation.....	757
Sarcoma, experimental, of bone.....	791	transplantation, technic.....	767
Scholl, A. J.: Review of urologic surgery.....	327, 922, 1090	Tendovaginitis: See under Tendons	
Scott, W. J. M.: Surgical treatment of bronchial asthma.....	1425	Testicles, carcinoma of.....	360
Serlinger, F. A. C.: Abscess of lung, with filling of a cavity and closure of a bronchial fistula by pedicle muscle graft; report of case.....	1313	tuberculosis of.....	360
Serotum, cavernous hemangioma of.....	829	undescended.....	1109
Seelig, M. G.: Bronchobiliary fistula.....	149	Thoracoplasty.....	1193
Seminal Vesicles, carcinoma of.....	360	and phrenicectomy.....	1545
tuberculosis of.....	360	Thorax, tumors, report on activities of registry.....	1121
vesiculitis.....	363	tumors, surgical treatment of.....	1679
Shoulder, fracture dislocation of.....	165	Throat, operative relief from pain in lesions of mouth, tongue and.....	143
recurrent dislocation of.....	766	Thrombo-angitis obliterans.....	735, 754
Singer, J. J.: Bronchobiliary fistula.....	149	Thrombosis and embolism.....	561
Bronchography.....	1571	Thyroid, gross and microscopic structure of, in man.....	986
Clinic demonstrations.....	1552	Tongue, operative relief from pain in lesions of mouth, throat and.....	143
Comparison of iodized oil and brominized oil.....	1660	Toxemia of intestinal obstruction, relation of adrenal gland to.....	272
Smith-Peterson, M. N.: Thirty-eighth report of progress in orthopedic surgery.....	154	Trachea, old nodular goiter surrounding trachea, posterior to carotid with isthmus posterior to esophagus; case with sudden death from acute abscess.....	466
Thirty-ninth report of progress in orthopedic surgery.....	752	changes in size and shape of tracheo-bronchial tree following stimulation of vago-sympathetic nerve.....	1577
Spinal Cord, loose cartilage from intervertebral disk stimulating tumor of.....	660	clin-ex camera studies of.....	1236
Spine, cervical, apparatus for reduction of fracture dislocations of.....	768	comparison of iodized oil and brominized oil in roentgenology.....	1660
curvature, investigation of adolescent kyphosis.....	167	Trauma to central nervous system, its effects on cardiac output and blood pressure, an experimental study.....	725
fractures of.....	162	genital.....	360
fractures, compression fractures of.....	768	genito-urinary.....	1111
fractures of transverse processes of lumbar vertebrae; report of 33 cases.....	968	of lip in children, extra-articular fusions of.....	766
fusion with osteoperiosteal graft.....	157	of seminal vesicles.....	360
tuberculosis, operative fusion for.....	765	of spine, operative fusion of.....	765
tuberculosis, roentgen diagnosis of.....	756	of testicle.....	360
Spleen.....	539	pulmonary.....	1562
Starr, F. N. G.: Endometrioma of terminal ileum, appendix and cecum.....	152	pulmonary, direct drainage of cavities.....	1161
Sternum, fracture and dislocation of.....	161	pulmonary, pathology and treatment.....	1122
Stomach, carcinoma of.....	550	pulmonary, phrenicectomy in 300 cases of.....	1169
cardiospasm.....	549	pulmonary, therapeutic pulmonary collapse in.....	1193
gastritis.....	546	renal.....	335
		roentgen diagnosis of.....	756
		roentgen diagnosis of Pott's disease.....	756
		Tumors: See also Cancer and under names of tumors	
		benign gastric neoplasms.....	551
		cells, cytology of serous effusions with reference to tumor cells.....	1672
		glant cell, and osteitis fibrosa.....	169
		of bladder.....	346, 1090
		of kidney.....	327, 927

INDEX TO VOLUME 19

Tumors—Continued	PAGE	PAGE	
of pleura and lungs.....	1567	Varicose Veins, oxygen content of blood with.....	898
of urethra.....	1106	Varney, P. L.: Bacterial flora of treated and untreated abscesses of lung.....	1602
Registry of Cl. st Tumors, report on.....	1121	Veins, pulmonary, air embolism from.....	567
surgical treatment of intrathoracic tumors.....	1679	surgical applications of therapeutic venous obstruction.....	1
Ureter, anomalies of.....	939	Verbrugge, J.: Review of urologic surgery.....	327, 922, 1090
infection of.....	343	Volkmann's Ischemia: See Contracture, Ischemic	
infection of stump.....	939	Vulva, fibroma of, containing an epithelial inclusion cyst.....	1061
obstruction of.....	941	Welles, E. S.: Phrenicectomy in 300 cases of pulmonary tuberculosis.....	1169
stones in.....	940	Wharton, L. R.: Primary carcinoma of fallopian tube; 14 cases.....	848
stricture.....	345, 943	Wilson, J. D.: Effects of closed pneumothorax and phrenicotomy on cardiorespiratory function.....	1205
Urethra, carcinoma of.....	364	Wilson, P. D.: Thirty-eighth report of progress in orthopedic surgery.....	154
congenital obstruction of prostatic urethra.....	1107	Thirty-ninth report of progress in orthopedic surgery.....	752
diverticula.....	367	Winslow, N.: Cavernous hemangioma of scrotum; report of case.....	829
diverticula in females.....	1108	Wounds, surgical, in human beings, a histological study of healing with practical applications; epithelial healing.....	835
stricture in male.....	1108	Wrist, dislocation of carpal semilunar bone.....	167
tumor.....	1106	traumatic osteoporosis of carpal bones....	156
Urinary Tract, malignant disease of.....	370	Yates, J. L.: Pulmonary tuberculosis, pathology and treatment.....	1122
Urine, antiseptics.....	371		
extravasation of.....	371		
sugar in, improved method of determining.....	1116		
Urologic Surgery.....	1114		
review of.....	327, 922, 1090		
Urologist and gynecologist, importance of closer relationship between.....	1116		
Van Allen, C. M.: Air embolism from pulmonary vein; clinical and experimental study.....	567		
Bronchogenic contamination in embolic abscess of lungs.....	1262		
Embolism in bronchogenic infection of lung.....	1279		
Van Dessel, A.: Thirty-eighth report of progress in orthopedic surgery.....	154		
Thirty-ninth report of progress in orthopedic surgery.....	752		